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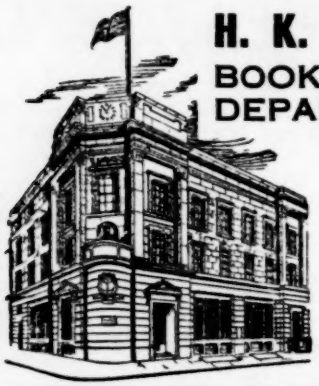

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BY A. E. WEBB-JOHNSON, C.B.E., D.S.O., F.R.C.S. Eng.
SURGEON TO THE MIDDLESEX HOSPITAL

IT would be difficult to exaggerate the terrible discomfort which a woman must suffer if she has a constant leakage from the vagina as the result of a fistulous communication with the urinary tract. The external genital anatomy of women provides no such convenient arrangement as that with which men are blessed, and the instrument maker has failed to produce an apparatus which will ensure a woman's comfort when she is suffering from urinary incontinence. It follows that she is generally dependent on primitive arrangements in order to absorb the leaking urine and save her clothes and the furniture of herself and her friends from damage. In addition to the discomfort which necessarily results—and this must amount to mental agony in a fastidious woman—the constant presence of a pad soaked in urine, which is often infected, sometimes leads to most distressing soreness of the genitals and thighs.

The surgeon is naturally distressed when he sees a patient in such a miserable predicament, but his distress is magnified a hundredfold when the state of misery is the result of an operation which has been embarked upon with confidence and hope.

The justification for confining my remarks to uretero-vaginal fistula lies in the fact that during the last 23 years I have had to deal with 23 of these cases, and have arrived at certain conclusions as to the best line of procedure in preventing and treating the condition. As I have stated, this serious condition is generally the direct result of surgical intervention. All my cases except one have been the result of a pelvic operation. In the odd one, which was the first I had to deal with, the fistula developed after a difficult parturition, protracted labour, and instrumental delivery.

Injury to the Ureter: its Prevention and Repair

Before considering the question of treatment it will be well to devote a little time to the discussion of the prevention of injury to the ureters and the steps to be taken at the time if the surgeon realises that damage has been done. The uterus, bladder, and lower ends of the ureters are in such close relationship, and the normal anatomical arrangement may be so distorted when the uterus is the site of a tumour, that it is not surprising that the ureter is injured sometimes. Hysterectomy is so frequently performed that one may say that the ureters are in danger almost daily in the hospitals of a large city. Accidental damage still occurs too frequently, and it should be the guiding principle of the gynæcologist that it ought never to occur. In cases of fibroid tumour of the uterus the accident may happen without being noticed, but in Wertheim's operation for carcinoma, in the course of which the ureters are isolated, and maybe their blood-supply imperilled, the surgeon is well aware of the risk being run and has the ureters under his direct observation. In a case of carcinoma it might be impossible to avoid damaging a ureter, but in the operation of hysterectomy for fibroids it should be one of the rarest of all accidents instead of one which is fairly common.

Twenty-one years ago Sir John Bland-Sutton opened a discussion on this subject at the Medical Society of London and the discussion made it clear that the ureters were often injured during the performance of abdominal hysterectomy. The injury may not be noticed. Bland-Sutton expressed the opinion that it is possible and probable that a ureter has been tied in the course of hysterectomy and the patient has recovered without anyone having a suspicion that such an accident has happened. It is indeed true that there may be no serious effect if the urinary tract is free from infection, but it is well to bear in mind that it may be some time before interference with the lumen of the ureters is revealed. I have recently had in my wards a case of nephrectomy for pyonephrosis in a woman who had a pelvic operation three and a half years ago. I doubt not that the obstruction to the ureter which was 1 inch from the vesical orifice was the result of the pelvic operation. While nephrectomy is never undertaken without the most careful investigation of the urinary tract, surgeons must be doubly cautious if the patient has had a pelvic operation.

The ureter has been deliberately tied after accidental division without untoward signs. Numerous gynæcologists have confessed to tying the ureter and dropping it back. This has only to be mentioned to be condemned. Bland-Sutton emphasised the importance of dealing with a cut ureter at the time. As he wittily pointed out—"Kidney tissue is very precious. Many persons get on very well in the world with very little brains and some with none, but no one can live without a certain amount of kidney."

CHOICE OF PROCEDURE

There are various alternatives open to the surgeon when faced with this accident, and it is very desirable that a surgeon who is exposed to the risk of injuring the ureter should be prepared at once to repair the damage. He may attempt end-to-end union or he may graft the ureter into the bladder or into the colon. This last procedure would only be permissible if the injury were high up and a portion of the ureter had been removed. Fortunately, the injury when it occurs is nearly always quite near the vesical end of the ureter. End-to-end union is far from satisfactory. Only when the conditions are very favourable can a satisfactory union be made between the divided ends of the ureter. Moreover, should any narrowing occur it would not be so easily recognised or corrected as in the case of a graft into the bladder. I do not hesitate to say that the surgeon's duty is to implant the divided end of the ureter into the bladder. Great care is required in the performance of this operation, for if plenty of room is not left for the implanted ureter it may become sclerosed by chronic ureteritis which may narrow and even obliterate its lumen. The narrowing may be a gradual process and the obstruction to the ureter may lead to serious hydronephrosis or pyonephrosis after an interval of years.

This risk of narrowing can be avoided or minimised by careful attention to detail. In the first place a useful little manœuvre is to pass long fine forceps along the urethra and make them protrude on to a selected spot on the posterior wall of the bladder. A small incision is made on to the end of the forceps and the ureter drawn into the bladder by a thread which has been attached to it. The ureter can then be sutured to the bladder wall outside and a water-tight junction established. This method of grafting is not so certain of success as making the junction

* An address delivered to the Manchester Surgical Society on Dec. 4th, 1934.

from inside the bladder. The surgeon need not hesitate to open the bladder during the course of an intraperitoneal operation.

If the bladder is opened and the ureter stitched in place from inside the viscus plenty of room can be left for the graft by leaving a gap below the suture line and passing a small drainage-tube through the posterior wall of the bladder into the retro-vesical tissues. The site of entry of the graft on the outside of the bladder can then be made extraperitoneal by suturing the pelvic peritoneum carefully over it.

If the bladder is not opened at the time and the implantation of the proximal end of the ureter is completed from outside the bladder the graft must generally be so closely sutured in position in order to make the junction absolutely water-tight that it is liable to become narrowed. If the implantation has been carried out in this way the graft should be kept under observation for some months and the opening of the ureter examined at intervals through a cystoscope. In this way any threatened contraction of the orifice, with the danger of damage to the kidney by obstruction and consequent increased risk of infection, can be recognised and dealt with either by dilating the orifice or, if necessary, by opening the bladder and improving the graft.

The surgeon may be labouring under the handicap that he is reluctant to call attention to the accident, but the interests of the patient demand that the graft should be kept under observation, and therefore the position must be faced and explained.

Treatment of Uretero-vaginal Fistula

I now pass to a discussion of the treatment of uretero-vaginal fistula. This may develop if the ureter has been cut and the injury has not been repaired, or if the blood-supply of the ureter has been so interfered with as to lead to sloughing of the lower end, or if the ureter or part of it has been included in a ligature or suture.

When it is noticed that there is a leakage of urine from the vagina the surgeon has first to ascertain from what part of the urinary tract the leakage is taking place.

First of all he must satisfy himself that the urine is not coming from the bladder. This is not so easy as one might expect. By careful observation and by the injection of coloured fluids into the bladder and ascertaining if any of the fluid finds its way into the vagina this point is however eventually cleared up. Being satisfied that the leakage is not from the bladder the surgeon must next ascertain from which ureter the urine is escaping. Fortunately he may easily get a very helpful clue to guide him in this investigation, for cystoscopy and the passage of a ureteral catheter may soon reveal the side on which the injury has been inflicted. The injured ureter is always obstructed whether it be completely divided or not. There is always obstruction to the passage of a catheter on the side of the fistula if it has been present a few weeks. This clue generally leads quickly to a definite diagnosis in cases following hysterectomy for fibroids, but in cases following Wertheim's operation the position is complicated by the fact that both ureters have been so disturbed and are embedded in such dense scar tissue on the floor of the pelvis that it is often difficult to pass a catheter into either ureter.

Eventually however—perhaps only after several attempts and with the use of very rigid ureteral catheters or bougies, reinforced with metal—a passage is found up one ureter while the other is found to be impassable. The side on which the obstructed ureter is found indicates the side on which the fistula is present.

In spite of the difficulties we may have to contend with in order to be absolutely sure on which side the lesion is situated, we are indeed fortunate compared with our forbears. A reference to Sir Henry Morris's Hunterian lectures delivered at the Royal College of Surgeons a short 36 years ago makes one realise the great advantages under which we work to-day. At that time it was computed that in any hundred hysterectomies, vaginal and abdominal, one or both ureters were tied or cut across in at least three. And Spencer Wells in 1881 stated that out of 94 published abdominal hysterectomies one ureter had been divided in six, and both ureters in two other cases. For these injuries nephrectomy was performed and in many instances healthy kidneys were removed. It would be bad enough to be misled as to the injured side at the present day and to proceed to expose the wrong ureter, but how tragic it must have been in the days of which Morris spoke, when nephrectomy was the accepted remedy and there were not the same facilities for diagnosis that we possess to-day.

In speaking of the difficulties experienced by surgeons trying to identify the kidney which was in connexion with the fistula Morris reported the following case:—

"A woman who had undergone vaginal hysterectomy by a distinguished gynæcologist recovered with an uretero-vaginal fistula. The patient was handed over to a distinguished general surgeon to be cured of this fistula. Efforts were made in a most careful manner to ascertain which ureter it was which had been wounded and become entangled in the vaginal cicatrix. These failing to afford definite information, the ureter of the suspected kidney was exposed through a lumbar incision and was temporarily ligatured. During this experiment, which was of course made under chloroform, no urine escaped by the vagina, but a certain amount was withdrawn by catheter from the bladder at the expiration of a given time. The inference was that the ureter temporarily ligatured was the one involved in the vaginal fistula; so the corresponding kidney was there and then excised. Imagine the surgeon's chagrin, and the patient's distress, the next day when it was discovered that, though she had lost a healthy kidney, the operation had not cured her of the fistula; for the wrong organ had been removed."

Having ascertained which side is affected what should be done next? In 3 out of my 23 cases I have had the good fortune to force a catheter up an obstructed ureter with removal of the obstruction, followed by closing of the fistula. This experience leads me to recommend that serious efforts should always first be made to dilate the obstructed ureter through the cystoscope if exploration gives the least sense of the ureteral catheter or bougie being engaged in a stricture. The surgeon may notice after prolonged efforts, perhaps with a ureteral bougie or catheter which has been made more rigid by metal being interwoven in its structure, that the instrument is not easily withdrawn, giving the same sensation as that experienced when a gum-elastic bougie has become firmly engaged in a urethral stricture but has not passed through it. Further efforts may result in the passing of the catheter and cure may be expected.

If disappointment attend these attempts then the bladder should be opened.

The best results are to be obtained by resecting the lower end of the ureter through the bladder up to the site of the fistula and suturing the ureter into the bladder at a point above the fistula. The great advantage of an approach through the bladder is that, when the implantation is made, ample room can be left for the grafted ureter and all danger of the development of a narrow orifice avoided. On opening the bladder the previous observations are confirmed by passing a catheter up the intact ureter. A catheter is then passed on the fistulous side up to the site of obstruction. An incision is then made round the lower edge of the ureteral orifice and continued up the bladder wall. The lower end of the ureter is identified and dissected up until the fistula is reached. The lower part of the ureter, including the fistula, is then

cut off and the divided end of the ureter is loosely sutured into the base of the bladder. A small drainage-tube is passed through the bladder wall below the implanted ureter into the retro-vesical tissues and fixed in position by a catgut suture, and a catheter is left in the ureter. The rest of the wound in the base of the bladder is closed and the bladder is drained through the suprapubic wound. The small tube draining the retro-vesical space is brought through the suprapubic wound and the ureteral catheter through the urethra. The ureteral catheter is removed in two days' time. The small tube is removed as soon as it becomes loose, and the bladder tube at the same time.

Convalescence is usually uneventful and the result a perfect and permanent cure. The operation is one of some delicacy and difficulty and takes some time to perform. It is more tiring and exhausting for the surgeon than for the patient, for in spite of the time it takes to complete the operation it is not associated with any shock.

This is what I consider the ideal way of dealing with these cases and in my opinion it should always be attempted. Sometimes it cannot be accomplished. This is more likely in the cases resulting from Wertheim's operation. After Wertheim's operation an incision through the base of the bladder leads into dense fibrous scar tissue in which it is always difficult and sometimes impossible to identify the ureter. If the surgeon fails to dissect out the ureter he should not hesitate to open the peritoneal cavity. He can then trace the ureter down to the floor of the pelvis and draw the lower end into the bladder through an incision in its posterior wall placed as low down as possible. It is helpful to attach a thread to the lower end of the ureter to assist in pulling it through into the bladder. The peritoneum over the pelvic floor should then be carefully sutured and the peritoneal cavity closed. The surgeon can then proceed to deal with the implantation of the ureter from inside the bladder as already described.

In some cases when the ureter is isolated it is found to be dilated. This need not deter the surgeon from proceeding with the implantation provided the patient has not shown symptoms of severe kidney infection. Unfortunately the patient may not reach the surgeon until signs and symptoms of renal infection are well marked—pyuria, pyrexia, and pyelonephritis, and perhaps pyonephrosis. In such cases nephrectomy is indicated unless symptoms subside rapidly under treatment with urinary antiseptics.

In four of my cases the kidney has had to be removed because pyonephrosis had developed. It has been indeed a Delian sacrifice and has led me to urge that these cases should be dealt with early, when there is much more likelihood that success will follow attempts at catheterising the ureter; operation, if necessary, will be easier than at a later date and the kidney will probably be saved. I have been able to pass a ureteral catheter on one patient comparatively easily when the fistula had only been present for a week and my colleague, Mr. E. W. Riches, has had a similar experience. Cure followed in both cases, though perhaps cure should not be attributed solely to this intervention as the leakage is sometimes only temporary. I have already mentioned cases in which I was successful in this manner and in one of these it was several weeks after Wertheim's operation. I still think, however, that the sooner the attempt is made after the development of the fistula the more likely it is to be successful. If the attempts to pass a ureteral catheter fail, operation for implantation of the ureter should not be proceeded with at once as the leakage may cease spontaneously, but operation should not be delayed more than a few weeks.

Conclusions

My experience leads me to the following conclusions: 1. All uretero-vaginal fistulæ should be dealt with as soon as possible after being diagnosed. 2. In the first place prolonged and even repeated attempts should be made to catheterise the ureters. 3. On the injured side obstruction is always found to the passage of the ureteral catheter when the fistula has been present for any length of time. 4. If catheterisation fails the implantation of the proximal end of the ureter into the base of the bladder by an intravesical operation gives the best prospect of cure. 5. This implantation can be successfully carried out if the case is seen early, but after Wertheim's operation it becomes increasingly difficult as time passes and dense scar tissue develops. 6. In the event of failure to complete the graft by an intravesical operation the peritoneal cavity should be opened, the ureter isolated, and the grafting operation begun from outside and completed from inside the bladder. 7. In seriously infected cases the best procedure is nephrectomy through a lumbar incision.

The cure of this unfortunate disability may require all the skill, patience, tact, and determination to succeed with which the surgeon may be endowed. When success attends his efforts he will receive deep gratitude from the patient who has been relieved of a condition which was making life almost unbearable. If the surgeon has succeeded in curing the patient without the loss of a kidney he will in addition have the satisfaction of knowing that he has left her not only relieved of her distress but still endowed with her full renal efficiency.

TREATMENT OF PUERPERAL FEVER BY ANTISTREPTOCOCCAL SERUM

SOME NEW EVIDENCE AND A RETROSPECT

BY LEONARD COLEBROOK, M.B. Lond.

MEMBER OF THE SCIENTIFIC STAFF OF THE MEDICAL RESEARCH COUNCIL; HONORARY DIRECTOR, BERNHARD BARON MEMORIAL RESEARCH LABORATORIES, QUEEN CHARLOTTE'S HOSPITAL, LONDON

FOR 40 years antistreptococcal sera have been undergoing clinical trial all over the world for the treatment of puerperal fever. They are still very extensively used, but no agreement has been reached by clinicians as to their value. Most observers have seen the occasional patient whose temperature dropped in dramatic fashion following the administration of antistreptococcal serum (possibly a "protein shock" effect, since this has sometimes happened with an infection which was not due to streptococcus); much more often they have seen the fever remit for a few hours only and the disease continue as before. It is not difficult to understand these discordant results and the many undoubted failures of serum therapy. The term "puerperal fever" covers a very wide range of pathological conditions—from localised infections of the genital tract, parametric cellulitis, and thrombophlebitis, to generalised peritonitis, "septicæmia" with or without metastatic foci, and endocarditis.

Critical judgment of the effect of any treatment will of necessity be very difficult in many of these conditions, for some of them—e.g., the infections which remain localised to the genital tract—carry a very high spontaneous recovery-rate (nearly 100 per

cent.); while in others—e.g., fully generalised peritonitis and endocarditis—it is hardly to be expected that any therapeutic agent could overtake the infection. Moreover, these varied pathological conditions are now known to be produced by very different microbes. The hæmolytic streptococcus is responsible for about half of them; anaerobic and other types of non-hæmolytic streptococci, *B. coli*, staphylococcus, and other organisms are responsible for the rest. There is no doubt (vide Table, p. 1087) that during all these 40 years antistreptococcal sera have very often been employed in circumstances which did not allow of a *specific* curative effect.

The sera themselves have varied considerably. For about 30 years following Marmorek's[1] work (1895) most workers aimed at producing a serum which was primarily *antibacterial*—i.e., one which would control the invasion of the tissues by the cocci. The possibility—and desirability—of producing an *antitoxic* serum was, however, not lost sight of (Marmorek, Aronson,[2] 1902), but the earlier attempts in this direction were not very successful. Since the war recognition of the fact that an exotoxin of the hæmolytic streptococcus ("Dick toxin") is produced in the human body—during scarlet fever, at any rate—and that this exotoxin can be neutralised, both in vitro and in vivo, by a highly antitoxic serum, has stimulated the hope that better therapeutic and prophylactic results might be achieved by such a serum than had been obtained with the antibacterial sera. The selection of good toxin-producing strains of streptococci for the immunisation of the horses, and the improvement of technical methods for the concentration of the antitoxic fraction of the serum, have given us sera of much greater potency than those of earlier days, and these sera have been extensively employed in the treatment of puerperal fever for the past ten years. Many reports of individual cases, or of very small series, have been published, but these are of very little evidential value. On a broad view it may be said that those who have had most experience have been least convinced as to the efficacy of these sera. An analysis of a large series of cases, treated and untreated, by Benson and Rankin[3] will be referred to later.

On the hypothesis that the toxins of puerperal fever strains might differ somewhat from those of scarlet fever, some laboratories have prepared sera from toxigenic puerperal fever strains.

Warnekros, Louros, and Becker[4] reported 200 cases of puerperal fever treated with such a serum without a death. The cases are described as severe (*schwere*) but the clinical data given are extremely scanty. We are not told whether there were any cases of peritonitis nor how many of septicæmia (hæmolytic streptococci in blood culture); nor indeed how many cases were infected by that microbe. Nor is there any estimate of the recovery-rate in a comparable series of unselected cases not treated by serum. From the fact that 4 of the 6 patients whose temperature charts are reproduced (presumably among the most severe) are stated to have had no microbes in the blood, while the 2 remaining cases grew respectively three and five colonies from the blood, it seems probable that a large proportion of the cases presented merely a localised infection which normally carries a recovery-rate of approximately 100 per cent.

In 1928 Gaessler[5] reported a further 400 cases from the same clinic with 20 deaths; 299 of his cases were admitted with little or no fever on account of difficult labours but subsequently became more or less febrile. In this series, as in the former, there was no distinction between cases infected by hæmolytic streptococci and those which were not, and the very meagre clinical data do not permit of any judgment as to the effects of the serum. Later reports do not seem to support these first claims to success.

Still more unsatisfactory as a statistical study is the analysis by Lash[6] (1929) of 57 cases treated with a similar serum made from puerperal fever strains. The death-rate among these cases was 32 per cent., but this compared favourably with that of a control group (treated in other ways) of 13 selected cases which showed a death-rate of 61 per cent. Fortunately details are given of these control cases, and it is seen that they comprise 8 cases of septicæmia and 7 of "peritonitis or beginning peritonitis"—scarcely a representative sample of ordinary puerperal infections.

In 1929 H. Vincent[7] introduced a "new" serum which has been extensively used in France. The method of its manufacture has not been disclosed, but there seems no reason to suppose that it rests on any new principle. No evidence has been given that it can either prevent or cure an infection by hæmolytic streptococci in animals, but in a recent paper Vincent[8] (1934) has claimed that by the use of enormous doses (1300 c.cm. in one child) no less than 180 (82·5 per cent.) of a series of 218 cases classed as "septicæmia and meningitis" have been cured. This remarkable claim demands careful examination. Such examination shows that there has not been personal observation of the cases. They have been collected from the numerous published reports of the medical press of France and other countries and of reports of cases sent to him privately. The published reports deal almost invariably with one or occasionally two cases of recovery, and they attribute that recovery unequivocally to the serum even when many large doses were required before the temperature fell. Frequently other forms of treatment were employed at the same time. These individual case reports tell us nothing at all about other cases treated who have not recovered.

In assessing the value of such evidence I think one should not forget that many medical men will publish individual successes while few will broadcast failures. It might well be that if *all* the cases of "septicæmia and meningitis" treated by this serum were faithfully recorded the result would be very different. Again, there is some doubt as to the sense in which Vincent uses the words "septicæmia and meningitis." He does not tell us categorically in how many cases hæmolytic streptococci were grown from the blood, nor in how many from the cerebro-spinal fluid, but he does mention in a footnote that some cases were included although their blood culture was negative. His claim that the recovery of the 180 cases was due to serum and not to "natural causes" appears to rest, however, on the summary statement that "Le septicémie à streptocoques comporte un pronostic fatal" (1929).*

That statement does not agree with my personal experience of hæmolytic streptococcal septicæmia (with positive blood culture). With Dr. R. Hare I[10] have reported (1934) 19 such cases (excluding cases of generalised peritonitis) observed during the years 1928–33 which showed a recovery-rate of 41 per cent.; and in a further series of 15 such cases observed during 1934 at Queen Charlotte's Hospital no less than 11 have recovered (73·3 per cent.). Seven of these 15 cases gave a positive blood culture on more than one occasion, and five of the seven recovered. In none of these cases was specific treatment used. The recovery-rate of 73 per cent. is probably quite unusual, but it serves to show how cautious one should be in attributing recovery in septicæmia to any particular remedy.

My impression after a careful study of these clinical reports—and of many which preceded them—is that none of them justify the conviction that antistreptococcal sera have really shown an indubitable

* In a later paper, 1934 (*b*), Vincent[9] admits that spontaneous recoveries from streptococcal septicæmia do occur but that they are "très exceptionelles."

effect upon the puerperal infections by hæmolytic streptococci. (I am purposely excluding scarlet fever from this survey, partly because I have no experience of it, and also because the rationale of treatment by an antitoxic serum in that disease is on quite a different footing.) If such a curative effect is to be clearly demonstrated in the human subject, it must be by application of the treatment to large groups of cases known to be infected by hæmolytic streptococci, and by critical comparison of their records with those of cases similarly infected but untreated. Both groups must be under the direct observation of the same individuals and the bacteriological data should be obtained in the same laboratory.

Investigations of this kind carried out for the first time during the last few years will now be described.

Benson and Rankin (1933) have reported upon 114 puerperal cases observed in Edinburgh. Half of them had received serum and half had not. The two groups comprise all the cases from whom a positive blood culture (hæmolytic streptococcus) was obtained during a period of several years. (It is important to note, however, that many of the serum-treated cases were only found to be "blood positive" at some period *after* the commencement of serum treatment.—Personal communication from Dr. Benson.) In 28 per cent. of them the treatment was commenced within 48 hours of the onset of fever. Of the 57 serum-treated cases 37 received scarlet fever antitoxin and 20 "puerperal antistreptococcus serum" (which also contained some antitoxin). The authors state that both sera were manufactured by Messrs. Burroughs Wellcome and Co. In 74 per cent. of the cases the serum was given intravenously as the makers recommend. The mortality-rate in the 57 serum-treated cases was 75 per cent. as compared with 68 per cent. in the control group. In view of the "several days of misery in the form of serum sickness," the great expense (nearly £300 for the 57 patients) and the absence of any evidence that the treatment had any beneficial effect, the authors recommend that the giving of serum "faute de mieux" ought to be discontinued.

Experience of Serum-treated Cases at Queen Charlotte's Hospital

Comparison of 69 cases treated with antistreptococcal or antiscarlatinal (antitoxic) serum before admission to Queen Charlotte's Hospital with other cases not so treated (1930-34).

CASES TREATED BY SERUM

Infected by hæmolytic streptococci	40 (58 per cent.)
Not infected by hæmolytic streptococci ..	29 (42 „ „)

ALL CASES OF PUERPERAL PYREXIA ADMITTED TO HOSPITAL

Infected by hæmolytic streptococci	60·8 per cent.
Not infected by hæmolytic streptococci ..	39·2 „ „

DEATH-RATE OF THE SERUM-TREATED CASES AND OF THE CASES WHO HAD NO SERUM

—	Cases	Deaths	Case-mortality (per cent.)
All cases treated with serum before admission	69	21	30·4
All cases who had no serum ..	932	108	11·6
Hæmolytic streptococcus cases—			
Treated with serum	40	18	45·0
Treated without serum ..	346	70	22·3

Antistreptococcal sera have not been used at the Isolation Block of Queen Charlotte's, but 69 cases during the last four years had been given serum before admission. Most of them were sent in by private doctors and they came from all parts of the Greater London area.

Certain data obtained from the records of these 69 cases—and of the cases who received no serum—are shown in the Table.

COMMENTS ON THE TABLE

(1) It is unfortunately not possible to give complete and entirely reliable data as to the exact kind of serum used in every case, its amount, or the route by which it was administered, because there was often difficulty in getting all these details from the doctor who sent in the case. So far as the records serve they show that the serum was always derived from laboratories of good repute; that 39 cases got "antistreptococcal serum" and 30 scarlatinal (antitoxic, concentrated) serum. One case had both. Thirteen cases had more than one dose. The amount of serum varied from 10 c.cm. to 140 c.cm. In most of the cases it was given intramuscularly.

(2) Since the 69 cases were treated by serum before admission to the hospital it is not possible to describe their condition at the time when the treatment was begun. In about 75 per cent. of the cases the first injection was given within 48 hours after the onset of fever—often within 24 hours. After admission to the hospital all cases were treated on precisely the same lines. Glycerin was usually instilled into the uterus several times daily for the first few days and the patient's strength maintained by good feeding and nursing. In the great majority no specific treatment of any kind was used.

(3) It will be seen that over 40 per cent. of the cases treated by serum were not infected by hæmolytic streptococci and were therefore subjected to the risk of serum sickness without any prospect of a specific immunising effect.

(4) The mortality-rates for the 69 cases treated by serum and for all cases who had no serum show a very big difference, but it would be a mistake to attach much importance to this, because these two groups are obviously unsatisfactory statistical material. Both include many cases not infected by hæmolytic streptococci and also a certain proportion of cases in which the fever was really of extragenital origin—e.g., cases of urinary infection, mastitis, bronchitis, and so forth. It is of interest to note in passing, however, that an examination of the published records of similar unselected cases of puerperal infection by a committee of the American Gynecological Society [11] in the early days of serum treatment (1899) gave very similar figures: 352 serum-treated cases showed a mortality three to four times as high as 138 cases which had no serum. The committee rightly recognised that the data were not entirely reliable and did not therefore permit of very emphatic statement of conclusions. Nevertheless it ventured the opinion that more patients were dying from the treatment than from the disease.

(5) The figures that merit most consideration are, of course, those showing the mortality-rates in the two groups infected by hæmolytic streptococci. Clearly it is difficult to deduce from them that the treatment by serum had any beneficial influence upon the infections—and this in spite of the fact that in 75 per cent. of the cases serum was given within 48 hours of the onset of fever—often indeed within 24 hours.

The important question remains, Did the serum actually, as the figures suggest, contribute to the unusually high death-rate among the 40 cases? This is such a serious issue that the data demand the most critical scrutiny.

I have considered the following possible sources of fallacy :—

(*a*) *That serum was given only to the cases who seemed most gravely ill.*—This consideration may well have been operative in a small number of the cases but not, I think, in a large proportion of them. My reason for that opinion is as follows: it is well recognised by all who have much experience of puerperal fever that the cases most gravely ill during the first week are those infected by hæmolytic streptococci. If serum had been reserved for these most severe cases one would expect to find a very high percentage (not less than 80 per cent.) of infections by hæmolytic streptococci among the 69 cases so treated. But only 58 per cent. were so infected—a figure actually a little lower than that for all cases admitted to the hospital. No less than 29 of the 69 cases, although they were given serum, had not an infection by hæmolytic streptococcus, and, as is usual in such cases, these 29 cases carried a low mortality-rate (10 per cent.). Moreover, a survey of the records of the 40 hæmolytic streptococcus cases treated by serum shows quite clearly that many of them were never gravely ill.

In my opinion therefore we must conclude that the whole 69 serum-treated cases represent just an average sample of febrile disturbances in the puerperium; and that most of them were given serum because they happened to be in the care of a medical man who believed that as soon as a woman developed fever in the puerperium it was best to employ that remedy. Even, however, if we suppose that 5 of the 40 hæmolytic streptococcus cases were given serum because the clinical condition was judged to be unusually serious, and that all the 5 died, there still remains a mortality-rate of 37 per cent. for the other cases whose selection was probably not determined by this special consideration.

(*b*) *That the 40 serum-treated cases were admitted on the average somewhat later than those who had no serum—and for that reason did not gain such benefit as may accrue from the routine treatment and specialist care in this hospital.*—It has been our experience that early admission—particularly of the cases infected by hæmolytic streptococci—is definitely correlated with a high recovery-rate. On working out the time of admission of the serum-treated and other cases, however, it does not appear that this consideration can have influenced the mortality-rates shown in the Table. The 69 serum-treated cases were admitted on the average 7·8 days after labour; the 40 hæmolytic streptococcus cases 8·0 days; the 18 fatal hæmolytic streptococcus cases 7·8 days; and 76 control cases, consisting of 19 consecutive cases chosen at random from each of the four years, 7·8 days.

(*c*) *That many of the infections among the 40 serum-treated cases had occurred in epidemics or during periods when the prevalent infections were of an unusually severe type.*—Actually only 4 of the 40 serum-treated cases originated in small epidemics (and 2 of them recovered). Both serum-treated and control groups were made up chiefly of sporadic cases spread over the four years. The mortality-rate among the 346 cases infected by hæmolytic streptococci never rose above 28 per cent. for any one year.

My opinion, after full consideration of these possible fallacies, is that the greatly increased mortality-rate in the serum-treated cases was due either to the serum having exerted an unfavourable effect—turning the scale against their recovery—or to the operations of chance. Choice between these alternatives is not easy. On the one hand, it is obvious that very many and very large doses of serum have been repeatedly given to human beings without apparent harm. On the other hand, evidence is not lacking which indicates that the injection of a foreign serum may sometimes be definitely prejudicial to infected human beings and animals. A. Jousset [12] (1924) and P. Courmont [13] (1934) have emphasised these adverse effects in connexion with experimental tuberculosis (guinea-pigs) and with phthisis in man.

The most striking evidence relating to streptococcal infections is that of Penfold and Butler [14] (1932), who observed that both normal horse serum and anti-streptococcal sera, given to mice at the same time as a dose of living streptococci, would sometimes hasten the death of the animals. The conditions in the infected human subject under treatment by serum are admittedly quite different from those of the mouse experiments and it does not therefore follow that the therapeutic sera will necessarily exert a similar effect in the two cases, but, until we have more understanding of the mechanisms involved, that possibility cannot be ignored. Pointing in the same direction is the recent warning by B. Schlesinger [15] (1935) against the danger of giving anti-streptococcal sera to children with acute rheumatism which in his experience is not infrequently "reactivated" by such treatment.

All this evidence, taken together with the well-known, but little understood, "toxic" effects of horse serum, ought, I think, to be taken into account before we subscribe to the dictum so often expressed that "a dose of serum can at any rate do no harm." Can we be sure that an agent capable of causing such profound disturbances as those associated with anaphylaxis, serum sickness, and agglutination of red corpuscles (the extreme degree of incompatibility between horse serum and human reds does not seem to have been generally recognised), will not sometimes have an adverse effect upon the complex mechanisms concerned in immunity to infective diseases? I would suggest that our view of serum therapy has in the past been somewhat unbalanced. We have focused attention too exclusively upon its antitoxic or antibacterial qualities and rather lost sight of the "toxic" potentialities which have to be set off against them. The possible benefits of passive immunisation probably must always be paid for. Sometimes, as in the case of diphtheria antitoxin, the price may be well worth while—in other cases, as perhaps in the case of anti-streptococcal serum, it may be too heavy.

At Queen Charlotte's, if we had given serum to all cases infected by hæmolytic streptococci, and if they had had the same death-rate as in the 40 cases so treated before admission (vide Table), there would have been approximately 86 more deaths than actually occurred during the years 1930–34.

Experimental Basis of Treatment by Anti-streptococcal Serum

It would not be profitable to set out in full the results of a critical survey of all the experimental work published in connexion with antistreptococcal serum, because so many points are left in doubt and require reinvestigation in the light of new knowledge about the group of hæmolytic streptococci. The following brief summary and references may, however, be useful :—

PROTECTION EXPERIMENTS

(1) By the immunisation of horses, rabbits, and sheep, sera have been obtained which, when given some hours in advance of the infecting dose, would protect mice and rabbits against 1000–100,000 M.L.D. of the strain used for immunisation (Marmorek, Bordet,[16] Aronson, Neufeld,[17] Simon,[18] Dochez, Avery, and Lancefield,[19] Yoshioka,[20] Lancefield and Todd [21]).

(2) It appears that these highly effective sera have only been produced with streptococcal strains of exceptional virulence, resulting from frequent passage through animals.

(3) Some of these protective sera were active against other strains of hæmolytic streptococci than that used for the immunisation of the horses (Sommerfeld,[22] Neufeld (1903), Simon); and it is possible (although not proven) that these other strains were sometimes of different serological type. On the other hand, the work of Dochez,

Avery, and Lancefield strongly suggests that the protection afforded by such sera is strictly type specific.

(4) It is not clear that the protective sera thus obtained by immunisation with highly virulent "passage strains" have ever been effective against strains of moderate or low virulence such as are habitually isolated from human infections—e.g., puerperal fever, surgical sepsis, &c.

(5) The mechanism of protection by the highly active sera has not been adequately established, but the work of Bordet, and particularly that of Neufeld and Rimpau,[23] seems to show that their capacity to render the very virulent streptococci susceptible to phagocytosis ("bacteriotropin effect") is a very important factor.

(6) Sera produced by the injection of toxigenic cultures of hæmolytic streptococci, or by filtrates of such cultures, into animals, are capable of neutralising that toxin both in vitro and vivo (Parish and Okell,[24] Hartley,[25] Pulvertaft [26]). When a potent antitoxic serum is injected into rabbits in advance of a large dose of an avirulent culture containing such toxin, the life of the animals is prolonged, or sometimes saved (by virtue of the neutralisation of the toxin), but infection of the tissues is not prevented (Parish and Okell). (It may be mentioned also that the active immunisation of human beings by Dick toxin does not render them immune to infections by hæmolytic streptococci—as judged by the incidence of tonsillitis among the immunised staffs of fever hospitals (Benson and Rankin,[27] 1934).)

(7) The commercial sera issued in recent years have at best only a very slight protective action against hæmolytic streptococci freshly isolated from acute septic infections of man even when they are given some hours in advance of the infection. When given at the same time as the infecting dose of streptococci they occasionally prolong the life of the test animals by a few days, more often they show no effect at all, and sometimes they definitely hasten death (Penfold and Butler).

CURATIVE EXPERIMENTS

Besredka [28] (1904) and Aronson (1905) record that a highly protective serum obtained by the immunisation of horses with a very virulent "passage strain" was able to overtake a rapidly fatal septicæmic infection of mice if it was given within 12–24 hours after the infecting dose of homologous culture. Repetition of the serum dose was sometimes necessary. Besredka's statement is the more precise. He says that 1/40–1/400 c.cm. of serum would suffice to save mice infected 18–24 hours previously with 2000 M.L.D. of culture.

I have failed to find evidence that the commercial sera now available have the slightest *curative* effect in infected animals.

IN VITRO EXPERIMENTS

The antistreptococcal and antitoxic sera at present available have not been shown to possess any bactericidal power. Hæmolytic streptococci will grow in them. Nor have these sera any power to promote the phagocytosis of virulent streptococci (bacteriotropin effect) (R. Hare [29]).

I believe it is correct to say that most of the laboratories producing these sera do not test them at all for any antibacterial (as opposed to antitoxic) properties.

Conclusions

1. There is no trustworthy clinical evidence that the administration of antistreptococcal serum for the treatment of human infections by hæmolytic streptococci has had any specific curative effect. (A possible effect on the *toxic* manifestations of scarlet fever is purposely excluded from this statement.)

2. The evidence obtained in puerperal fever cases at Queen Charlotte's Hospital suggests that such administration may sometimes have an *unfavourable effect* upon puerperal infections by hæmolytic streptococci; and this impression is to some extent supported by the evidence of animal experiments. All our experience carries the lesson that it is in the best interest of the patient suffering from an infection by hæmolytic streptococci not to interfere with her immunising mechanisms (about which we know so little as yet) until we can be sure that such interference does not do harm.

3. Although sera have been produced which would protect animals against infection by streptococci of artificially enhanced virulence, there is no satisfactory evidence that a serum has ever been produced which would afford more than very slight protection (occasionally) against hæmolytic streptococci freshly isolated from acute human infections and of various serological types.

4. Similarly there is no evidence that any antistreptococcal serum has ever exerted a *curative* effect in animals infected by such hæmolytic streptococci freshly isolated from human infections.

5. It is a matter for regret that antistreptococcal sera should have been issued for clinical trial so long before satisfactory experimental evidence as to their curative effects in animals was available—or a strong presumption existed (from unequivocal in vitro experiments) that such a curative effect would be obtained in man. Until our knowledge of immunisation against the hæmolytic streptococci has progressed further it would seem desirable to discontinue the use of antistreptococcal sera in the treatment (and prophylaxis) of puerperal fever and "surgical sepsis."

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WORTHING HOSPITAL.—The governors of this hospital, with the financial support of the borough council and the West Sussex county council, have authorised the preparation of plans for a maternity block designed as a self-contained unit with independent lighting and heating systems. Of the ten beds to be provided, half will be at the service of the borough and county councils. The building is to be planned so that the number of beds may be increased to 16. The patients will be nursed by a staff of fully qualified midwives who will be lodged and boarded on the new premises. The proposed cost is £12,000. Of this sum, £8000 is either in hand, or promised, including £1000 from each of the two councils. The accounts of the hospital for the year showed a deficit of £630, and if £2010 received from legacies had not been put into revenue the debit balance would have amounted to £2640.

FURTHER STUDIES ON THE ÆTIOLOGY OF ACUTE RHEUMATISM

By Bernard Schlesinger, M.D. Camb., F.R.C.P. Lond.

PHYSICIAN TO OUT-PATIENTS, HOSPITAL FOR SICK CHILDREN, GREAT ORMOND-STREET, LONDON

A. Gordon Signy, M.B. Lond.

ASSISTANT PATHOLOGIST AND RESEARCH FELLOW AT THE HOSPITAL; AND

W. W. Payne, M.B. Lond.*

BIOCHEMIST TO THE HOSPITAL

(From the Hospital for Sick Children and from the Children's Heart Hospital, West Wickham)

The search for a causal bacterium in acute rheumatism is at present mainly concentrated upon the hæmolytic streptococci. A direct demonstration that these organisms are constantly present in rheumatic inflammatory lesions would be convincing, but the results of different workers are not in agreement. This divergency has led to other methods of approach to the problem. In most of the recent investigations the search for bacteria in the affected tissues is abandoned and the indirect method of demonstrating immunity reactions to hæmolytic streptococci is employed.

Agglutination, complement-fixation, and precipitin reactions have all been used for this purpose (Coburn and Pauli, 1932). Even more delicate and specific are the tests for antihæmolysin (Todd, 1934; Griffiths, 1934), antistreptolysin (Myers and Keefer, 1934), and antifibrinolysin (Hadfield, Meager, and Perry, 1934). It is important to realise, however, that these immunity reactions are not specific to rheumatism but appear in the blood during convalescence from scarlet fever, erysipelas, acute streptococcal tonsillitis, and indeed after any acute streptococcal infection. Similar reactions in patients with acute rheumatism cannot then be taken to indicate anything beyond proof of a recent infection with hæmolytic streptococci.

In a previous communication (Schlesinger and Signy, 1933) we showed that it was possible to demonstrate streptococcal precipitins in the blood of rheumatic patients two to four weeks after the onset of a nasopharyngeal infection. The time at which these appeared thus corresponded to the end of the "silent period." The type of precipitin produced corresponded to the type of streptococcus responsible for the throat infection, although a certain amount of cross-precipitation occurred. Cases which relapsed with acute rheumatism gave the most marked precipitin reactions, and the question was raised whether a positive precipitin reaction might not be taken as an indication that a rheumatic relapse was to be expected. Here the matter was left to await further research into the whole question of precipitin formation following streptococcal tonsillitis.

Present Investigation

Our previous experiments were conducted with filtered saline extracts of ground-up streptococci ("endotoxin"). A natural presumption was that certain constituents of the bacterium would be found to have particularly strong precipitogenic properties. The present investigation deals with this problem, and also attempts to discover the principal factors involved, particularly in what way the reaction might be peculiar to acute rheumatism.

Of the various bacterial parts the carbohydrate fraction of the streptococcus has been consistently found to possess such poor antigenic properties that we have concentrated on the protein fractions. By the process described in the Appendix to this paper, two distinct nucleoprotein fractions were obtained—an acid and an alkaline extract—and precipitin reactions carried out with each. These extracts were derived from the following three organisms, and tests were performed with each, as far as possible in the same patient for the sake of comparison.

1. A hæmolytic streptococcus obtained from the throat of a patient with virulent rheumatism "(Carter streptococcus"), hereafter referred to as H.S.
2. A scarlet fever streptococcus, hereafter referred to as S.F.
3. A *Streptococcus viridans* obtained from the blood culture of a case of subacute bacterial endocarditis, hereafter referred to as V.

Tests were also carried out with the globulin and albumin fractions obtained, undenatured, from ground-up cocci. (See Appendix.)

In the first series of experiments 30 rheumatic patients were investigated after an attack of acute pharyngitis which was not followed by a definite rheumatic relapse. The patients' sera were tested for precipitins at intervals during a period of two or three months, using the technique described in our previous paper.

After a while it was noticed that nucleoproteins prepared from different batches of the same cultures of streptococci varied in their antigenic properties, although the technique used in their manufacture was identical. This meant that a series of comparable precipitin reactions in one patient could only be expected if the same batch of antigen were employed throughout.

PRECIPITIN REACTIONS IN RHEUMATIC PATIENTS FOLLOWING ACUTE TONSILLITIS OR PHARYNGITIS

In 9 out of the 30 cases the results obtained were considered unreliable owing to the reason just mentioned. In the remaining patients the same batch of nucleoprotein (Batch L) was used throughout in 15 cases and another batch (Batch 1A) throughout in a further 6 cases (see Table I.).

Table I.—*Precipitin Reactions*

—	Nucleoprotein.		Total.
	Batch L	Batch 1A	
Number of cases	15	6	21
Positive reactions	12	6	18
Negative reactions	3	0	3
Time of appearance following acute tonsillitis—			
(1) Between 10th and 30th day	9	3	12
(2) During 1st week	3	3	6
Final precipitin test—			
(1) Precipitin absent	10	4	14
(2) Precipitin still present	2	2	4

Throat cultures taken during the attack of acute tonsillitis showed the presence of hæmolytic streptococci almost invariably except in the three patients with negative precipitin reactions, from whom indifferent streptococci unrelated to the three antigens used were cultivated. The time at which precipitins appeared in the blood stream is of some interest. In

* All working with a grant from the Harmsworth Research Fund.

12 of the 18 cases the characteristic immunological response developed during the second and third weeks after infection. In the remaining 6, precipitins were found present very shortly after the tonsillitis, during the first week. Two opposite types of reaction were observed in this last group :—

(1) An increasing degree of precipitin formation during the four consecutive weeks following the tonsillitis (3 cases).

(2) The strongest reaction observed immediately, waning during the ensuing weeks (3 cases).

This observation and also the fact that precipitins usually disappeared in the end suggest that the reaction, although present early, was again an immunological response to the preceding tonsillitis and not an inherent property of these sera. As a rule precipitin was only demonstrable for a period of one month, but in one or two cases it persisted for several months. Occasionally a return of precipitin was noted two to three months after the tonsillitis, long after the original reaction was over and the patient's serum had been negative for some time. Such instances are not included in the analysis just given and their significance is not understood.

DETAILS OF PRECIPITATION

Reference has already been made to the varying potency of the different antigens used. Details of the individual tests which follow (Table II.) make it quite apparent that the acid nucleoprotein extract of the "Carter" hæmolytic streptococcus (HS.D.) gave the largest number of precipitin reactions. Tests with bacterial globulin and albumin showed that both components have antigenic properties, although the globulin element appeared to be the more potent. It is interesting to note that when doing skin tests with these extracts, the best reactions were obtained with the alkaline extract (HS.E.).

TABLE II.—*Details of Tests*

Case.*	Throat culture. (tonsillitis.)	Antigens. HS.D.	HS.E.	SF.D.	SF.E.	V.D.	V.E.	A.G.
1	Hæm. strep.	+	+	+	..	..	..	..
2		+	..	..	..	..	..	tr.
3		+	+	..	..	+	..	..
4		+	..	+	..	..	..	..
5	Hæm. strep. and *viridans* strep.	±	..	..	..	..	..	..
6		+	..	..	..	..	..	..
7		+	+	..	..	..	..	+ +
8		tr.	+	..	..	..	..	..
9	Hæm. strep.	+	..	..	..	+	..	..
10	*viridans* strep.	tr.	..	..	..	+	..	..
11	Hæm. strep.	+	..	..	..	..	..	+
12	Hæm. strep. and *viridans* strep.	+	..	..	..	..	..	+ +
13	Hæm. strep.	±	..	..	..	..	..	..
14		+	..	..	..	..	..	..
15	†	+	..	±	+	..	..	..
16	Hæm. strep.	+	..	..	..	±	+	± ±
17		..	..	..	..	±	+	± ±
18		+	..	..	..	..	..	..

* Rheumatic.

Abbreviations.—H.S.= hæmolytic streptococcus (Carter). S.F.= scarlet fever streptococcus. V.= *viridans* streptococcus from malignant endocarditis. D.= acid nucleoprotein extract. E.= alkaline nucleoprotein extract. A.= albumin extract. G.= globulin extract.

+ = positive. ± = slight positive. tr. = trace.

A certain amount of cross-precipitation was observed, for positive reactions occurred with antigens other than those obtained from bacteria isolated from the throat at the time of the tonsillitis. With one exception, whenever precipitins to HS.D. or E. were found present in the patient's serum, the preceding tonsillitis had always been a hæmolytic streptococcal infection. Positive precipitin reactions with V.D. or E. antigens were not necessarily associated with a previous *Streptococcus viridans* infection of the throat. Occasionally precipitin reactions were produced by the S.F. antigen as well as the H.S. antigen.

CONTROL EXPERIMENTS

Two sets of experiments were undertaken. In the first of these the sera of different groups of people were tested against the nucleoprotein of organisms other than streptococci. For this purpose *B. coli* and *Staphylococcus aureus* were chosen, and antigens were prepared from these with the standard technique. Presumably because of the universal distribution of these organisms, positive precipitin reactions were obtained in most of the subjects tested (Tables III. and IV.). These cannot therefore be regarded as suitable controls. Nevertheless they have been included since they form a striking comparison with the negative results obtained with streptococcal antigen in normal non-rheumatic subjects.

TABLE III.—*Precipitins to* B. coli

Subject.	Numbers tested.	*B. coli* D (acid extract). Pos.	Neg.	*B. coli* E (alkaline extract).
Laboratory staff ..	6	6	0	Negative.
Rheumatic patients ..	3	2	1	,,
Scarlet fever patients	7	2	5	,,

TABLE IV.—*Precipitins to* S. aureus

Subject.	Numbers tested.	*S. aureus* D (acid extract). Pos.	Neg.	*S. aureus* E (alkaline extract).
Laboratory staff ..	6	4	2	Negative.
Rheumatic patients ..	2	2	0	,,
Scarlet fever patients	6	5	1	,,

The second series of control experiments was concerned with streptococcal precipitin reactions in different groups of individuals. It attempted to assess the relative importance of rheumatism and tonsillitis in this connexion. There were four groups as follows : (1) patients with quiescent rheumatism unassociated with acute tonsillar infection ; (2) non-rheumatic subjects ; (3) non-rheumatic individuals following a recent tonsillitis ; (4) scarlet fever patients. The results of the experiments on these four groups have been summarised below.

1. *Control patients with quiescent rheumatism.*—A total of 13 patients were tested for precipitin reactions with streptococcal nucleoprotein, and the results were :—

Negative to H.S., S.F., and V., both to D. and E. antigens	8 cases.
Slightly positive to HS.D	4 ,,
Positive to HS.D	1 case.

From this it would appear that in the absence of tonsillitis streptococcal precipitin formation is neither very common nor well marked.

2. *Non-rheumatic patients (surgical cases).*—In this group 16 cases were tested :—

Negative to H.S., S.F., and V., both to D. and E. antigens	12 cases.
Slightly positive to HS.D	2 ,,
Slightly positive to V.D.	2 ,,

Non-rheumatic persons thus showed only a few slight positive reactions.

3. *Non-rheumatic patients following tonsillitis.*—When, however, another similar group of non-rheumatic patients

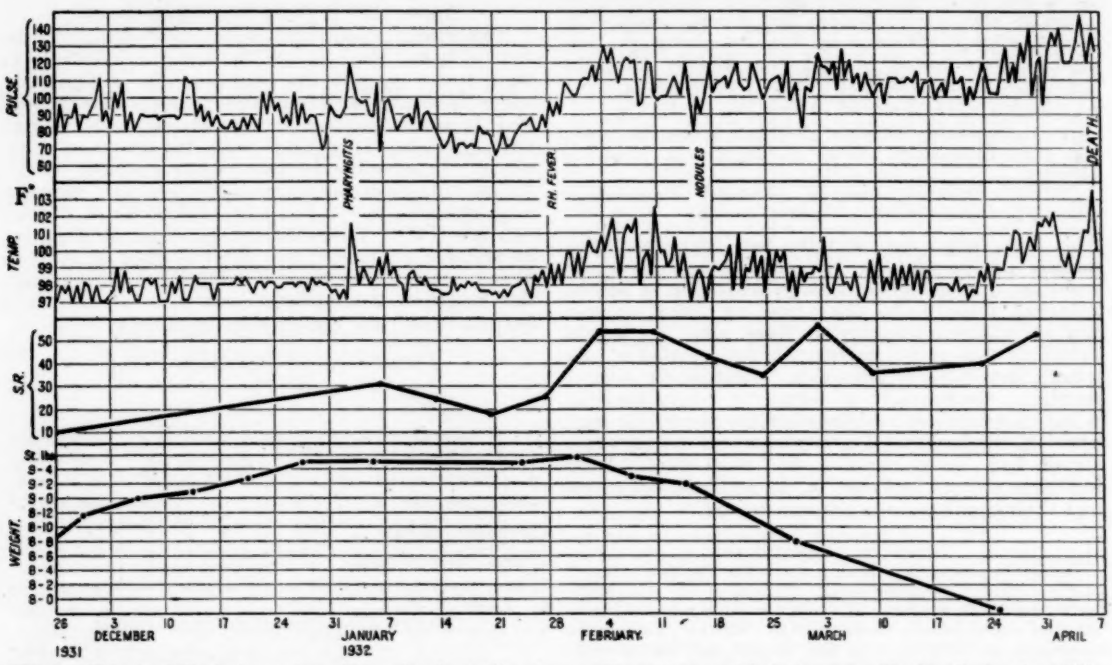

FIG. 1.—This chart illustrates various stages of a rheumatic relapse. The patient, a girl of 14 years, with old mitral endocarditis, was in a quiescent stage, afebrile, with a normal pulse-rate and steadily gaining weight. Her tonsils had been removed; nevertheless, following an acute pharyngitis and a "silent period" of three weeks, active rheumatism set in with fever, pericarditis, and later, the appearance of subcutaneous nodules. Note the sudden increase of the sedimentation-rate (S.R.) and the synchronous rapid loss of weight until death supervened.—From "Recent Progress in Medicine and Surgery," edited by Sir John Collie, chapter on Rheumatism by Schlesinger. London. 1933.

were tested shortly after an attack of acute tonsillitis, half of them gave positive reactions at the appropriate time—though the numbers are too small for comparison. The 6 cases gave the following results:—

Positive to HS.D., SF.D., and SF.E. between 10th and 18th day (neg. 24th day) ..	1 case
Positive to SF.D. between 10th and 18th day (neg. 24th day)	2 cases.
Negative throughout	3 ,,

4. *Scarlet fever patients.*—We are indebted to Dr. Wilfrid Sheldon for the results of a series of precipitin tests performed on the sera of his scarlet fever patients shortly after the onset of the disease. In the 30 cases the results were:—

Positive to SF.D. (3 of them also positive to SF.E.)	14 cases.
Positive to HS.D. (2 also positive to HS.E.)	5 ,,
Slightly positive to HS.D.	2 ,,
Positive to HS.E. only	3 ,,
Slightly positive to V.E.	2 ,,
Negative to SF.D.	16 ,,
Negative to SF.E.	27 ,,

Thus precipitins were demonstrated in the blood of about half of these patients. Reactions with the scarlet fever streptococcal antigen were obtained frequently in this group alone, a fact that is perhaps not surprising, and lends support to the view that these reactions are largely specific.

Finally a comparison was made between the sera of rheumatic and non-rheumatic patients with and without a preceding tonsillitis in regard to precipitin formation against the globulin and albumin fractions of hæmolytic streptococci. Positive results were most often observed in rheumatic patients following tonsillitis. This is not surprising, since it is in these cases that a reaction with the unsplit nucleoprotein antigen is most frequently obtained. The results of these experiments are given in Table V.

TABLE V

Precipitin Reactions to the Globulin and Albumin Fractions of Streptococcus hæmolyticus. (36 cases tested.)

—	Cases.	Pos. G. and A.	Pos. G.	Pos. A.	Neg. G. and A.
Rheumatism—					
With acute tonsillitis ..	12	6	4	0	2
Without acute tonsillitis	11	0	1	0	10
Non-rheumatic cases—					
With acute tonsillitis ..	3	0	1	1	1
Without acute tonsillitis	10	2	2	1	5

Abbreviations.—G. = antigen obtained from globulin fraction. A. = antigen obtained from albumin fraction.

Discussion

It has already been emphasised that precipitins to hæmolytic streptococci can be demonstrated in a number of non-rheumatic conditions. The investigations here recorded indicate that precipitin formation in acute rheumatism depends more upon the preceding tonsillitis than upon the rheumatic process itself. The sera of patients with quiescent rheumatism unassociated with a recent throat infection were almost consistently negative. On the other hand, tonsillitis in a proportion of non-rheumatic subjects was also found to provoke precipitin formation at a time and to a degree strictly comparable to that observed in rheumatic patients. Notwithstanding this, we were impressed with the more constant reactions which occurred among the latter, and it would be no exaggeration to say that rheumatic patients appear to react more strongly to acute streptococcal infections than do other people. Our researches prove no more than this. At the same time they give some indication that the various

immunological responses, such as the formation of precipitin, antihæmolysin, antifibrinolysin, &c., in acute rheumatism are all probably the direct outcome of an acute streptococcal nasopharyngeal infection. It is well recognised that such an infection may be present without symptoms and thus go undetected. That it may be followed two to four weeks later by acute rheumatic manifestations is also well known (Schlesinger, 1930). In the latter event, the antistreptococcal reactions discovered in the patient's serum might be interpreted as proof that the acute rheumatism is a direct result of infection with hæmolytic streptococci. This assumption may be correct, but is not justifiable from this evidence alone.

To our minds one of the most important and interesting features of rheumatic disease is the "silent period." A clear explanation of the interval of ten to thirty days which intervenes between a rheumatic relapse and the preceding streptococcal tonsillitis would add considerably to our knowledge of the ætiology. The fact that changes in the patient's blood, such as precipitin formation, are also at their height at the end of that period and just when the relapse is to be expected must have a distinct significance. The association has been explained on an allergic basis, but the reasoning is not clear or satisfactory.

On the evidence of these serological reactions it might be assumed that the patient's immunity to streptococcal infection is at its height at the end of the "silent period." Careful inquiry, however, reveals that it is just at this time that localised inflammatory lesions are likely to occur throughout the body. This is obviously the case with regard to acute rheumatism (Fig. 1). The complications of streptococcal tonsillitis in general also point to the fact that the patient appears to be particularly vulnerable at the time when the early serological changes are at their height, that is, during the second and third weeks.

"SILENT PERIOD" IN DISEASES OTHER THAN RHEUMATISM

The four examples that will be given are otitis, meningitis, adenitis, and nephritis. Some of these disorders are frankly pyogenic in nature, but whether they can be explained as a direct extension of the original infection or need some other interpretation, the same "silent period" is found in them all. It is shortest in *otitis* following tonsillitis, being then more often a week or ten days (Fig. 2). Otitis may also follow tonsillectomy, and in this case the intervening period is usually longer.

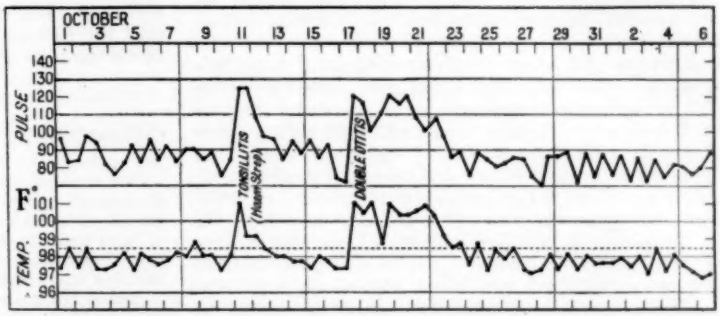

FIG. 2.—The chart in a case of streptococcal tonsillitis complicated by otitis media, demonstrating a similar although shorter silent period to that seen in Fig. 1.

The silent period in streptococcal *meningitis* is not generally realised, but deeper inquiry into the history of such cases will almost always elicit the same story. So constant is this that it becomes almost pathognomonic of the disease. The illness begins with an acute nasopharyngeal infection, followed in about a week by an extension to the middle ear. Here the inflammation may gradually subside spontaneously or require relief by paracentesis. After this the temperature falls to normal, and the patient appears to be well on the road to recovery. The picture then changes abruptly, when three weeks from the

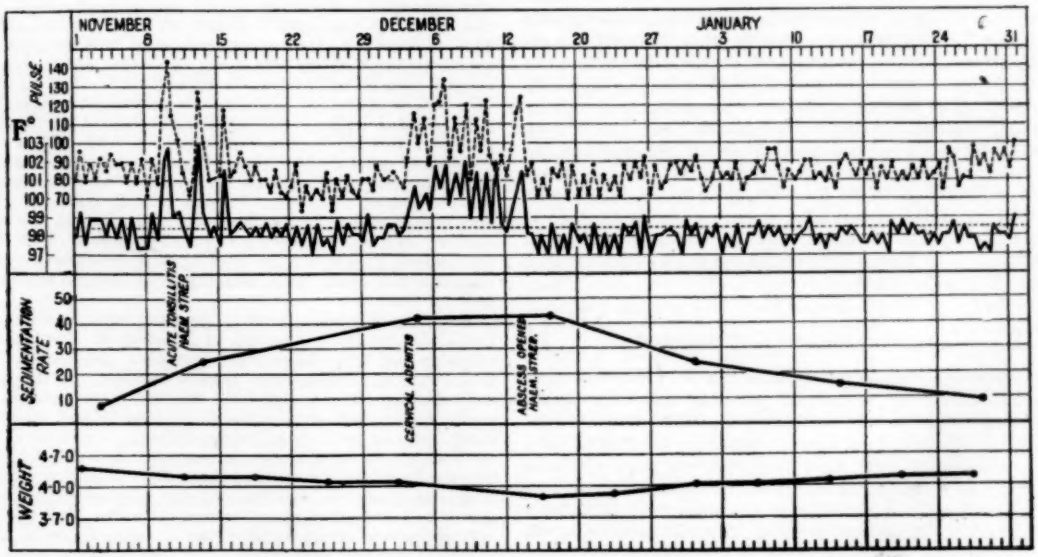

FIG. 3.—Cervical adenitis following a hæmolytic streptococcal tonsillitis with a well-marked intervening silent period.

onset of the otitis there is a sudden renewed pyrexia with signs of cerebral irritation. This soon gives way to evidence of frank meningitis, and the condition generally terminates fatally.

These are two examples of delayed pyogenic complications in close connexion with a primary focus of infection.

Cervical *adenitis* may either become purulent or stop short of this and heal without interference. In either event the same remarkable intervening period occurs (Fig. 3).

Nephritis following simple streptococcal tonsillitis or scarlet fever resembles acute rheumatism in being seldom pyogenic. Again there is the delay of two or three weeks before it arises. Suspecting that there might be changes in the kidneys short of actual nephritis following acute streptococcal throat infections, we have investigated 20 rheumatic patients with this point in view. In a large proportion of those examined it was found that a varying degree of albuminuria appeared in the urine, sometimes associated with red and white blood-cells, from the tenth to the twenty-first day after the onset of tonsillitis. The urine was examined daily for over a month both by heating and by the salicyl sulphonic acid test. Ten rheumatic patients without tonsillitis were also investigated as controls. In a number of these, albumin was found to be present at various times, but not persistently over a given period, and only for a day or two at a time. Among the controls the albuminuria was never associated with red or white cells in the urine. Catheter specimens were taken in a few cases from both series and the urine cultured. These were found to be sterile, and throughout the investigation streptococci were not discovered on microscopic examination of the deposits obtained by centrifuging the urine. These slight renal inflammatory changes following throat infections are not confined to rheumatic patients. De Wesselow (1932) made a similar investigation of 134 patients who were recovering from an attack of tonsillitis and found albuminuria in a considerable proportion of them.

It appears therefore that the widespread results of an acute streptococcal throat infection can be recognised both in rheumatic patients and in those who show no evidence of a subsequent rheumatic process. Some of these results may become manifest after a latent period, and at the time when the immunity response to the original infection is at its height. The tissues at that time appear to be particularly vulnerable and it is possible that this allows some as yet undiscovered cause of rheumatism to enter the body; or perhaps this state of increased susceptibility permits an already present but latent causal agent to enter into a state of activity. It is conceivable that a virus may be the answer to the problem, and we are investigating the disease further from this point of view.

Summary and Conclusions

(1) Streptococcal precipitins can be demonstrated in the blood of rheumatic patients following acute streptococcal throat infections. The most usual time of their appearance is between the tenth and thirtieth days. (2) The nucleoprotein and globulin fractions of the bacterial substance provide the best antigens for demonstrating the reaction. (3) Although the reaction seems to be most frequent and strongest in rheumatic subjects, it is not confined to them. Tonsillitis in non-rheumatic patients may give rise to the same sequence of events. (4) Rheumatic relapses are commonest from ten to thirty days after a streptococcal tonsillitis—i.e., at a time when changes in the patient's blood, such as precipitin formation—are at their height. (5) The presence of a similar "silent period" in various complications of streptococcal tonsillitis is reported and its general significance is discussed. (6) The relationship of hæmolytic streptococcal infection to acute rheumatism is reviewed, and mention is made of the possibility that the disease is caused by some additional specific factor such as a virus.

Appendix

PREPARATION OF NUCLEOPROTEIN EXTRACTS (HEIDELBERGER AND KENDALL, 1931)

Cultures of organisms obtained in a medium of glucose phosphate broth at a pH of 7·8 were centrifuged. The deposit was washed in saline and suspended in 200 c.cm. of acetone. It was then shaken mechanically for two hours, centrifuged, resuspended in the same quantity of acetone and allowed to stand overnight.

After being centrifuged again the organisms were suspended in 200 c.cm. of ether which had previously been freed from alcohol, peroxides, and aldehydes by washing with water, drying with calcium chloride, and storing in the dark over calcium chloride and sodium hydroxide pellets. The suspension was then stirred frequently for several hours, again centrifuged, and this process repeated with a fresh quantity of purified ether. A final amount was added and the mixture was allowed to stand overnight, after which it was centrifuged and the organisms were dried in vacuo over phosphorus pentoxide. The defatted cells were ground in a ball mill at room temperature until no intact cells could be observed in a smear stained by Gram's method.

The ground material was then rotated in the ball mill with a little 0·2 normal acetate buffer solution at pH 4 for 10 minutes and rinsed into about 200 c.cm. of the same buffer solution and shaken mechanically for 5–6 hours. All these operations were performed in the cold. The mixture was then centrifuged. The supernatant was saved and was tested for specific polysaccharide.

The residue in the centrifuge tube was ground in a mortar with a little chilled M/15 phosphate buffer solution at pH 6·5, and added to about 200 c.cm. of the same solution and shaken mechanically for 5–6 hours. The mixture was centrifuged until clear, and the supernatant was removed and acidified with glacial acetic acid until the resulting precipitate began to flock (Fraction D). The residue in the centrifuge tube was ground and extracted with about 200 c.cm. of water, adding enough normal ammonium hydroxide from time to time to maintain pH at 8·4—i.e., just pink to phenolphthalein. The mixture was again centrifuged and cleared as much as possible, and the supernatant acidified with 50 per cent. acetic acid until the precipitate began to flock (Fraction E). Supernatants of Fractions D. and E. were tested for carbohydrates. Fraction D. was homogenised in about 50 c.cm. of water and redissolved with the aid of chilled normal sodium bicarbonate solution which had been neutralised to pH 6·8 by cooling and cautiously adding glacial acetic acid. Care was taken to leave Fraction D. acid to litmus.

Fraction E. was similarly treated, using ammonium hydroxide instead. The pH of Fraction E. should never overstep pH 8·5. After reprecipitation, Fraction D. was dissolved in neutralised normal sodium bicarbonate, centrifuging off any insoluble residue, if necessary. To this solution sufficient 5 per cent. phenol was added to make 0·5 per cent. final concentration. Fraction E. was redissolved in a minimal amount of N/10 NaOH and centrifuged. To the residue more N/10 NaOH was added and the mixture centrifuged, the supernatants being saved and carbolised as in Fraction D. The total nitrogen was estimated in both solutions D. and E. by a micro Kjeldahl method and diluted for use to a concentration of 20 mg. of nitrogen in 100 c.cm.

Both these fractions consist of nucleoprotein. Fraction E. is relatively stable, but Fraction D. is very easily broken down into simpler substances, and even slight increases in the pH of the solutions are capable of bringing this change about. It was found almost impossible to maintain the exact pH of the neutralised sodium bicarbonate solution owing to loss of CO_2 with slight rises of temperature or even rough handling. This is the cause of the varying potency of the D. fragment. In regard to the bacterial fragments it would seem that the less the protein complex is broken up, the greater is its antigenic power. This is also shown by the larger moleculed globulin fraction having a greater antigenic power than the smaller moleculed albumin fraction.

PREPARATION OF ALBUMIN AND GLOBULIN FRACTIONS (GOUGH, 1933)

Twenty litres of a 24-hour culture of hæmolytic streptococci, grown in glucose phosphate broth, was centrifuged and the deposit desiccated over concentrated sulphuric acid in vacuo for two days. The dried organisms were then transferred to a ball mill and ground until no intact organisms could be seen in a stained smear.

The contents of the ball mill were then extracted with 500 c.cm. of distilled water by shaking for 2–3 hours and then centrifuged and the supernatant fluid removed. The deposit was again shaken with 200 c.cm. of water and recentrifuged, and the supernatant fluid removed and added to the first fluid. This was repeated until only a little insoluble material was left. The supernatant fluids were then saturated with ammonium sulphate. After a short time a curd appeared, consisting of the precipitated proteins. The whole was filtered and the curd saved. This greyish curd was washed into about 100 c.cm. of distilled water, shaken vigorously, and refiltered. This process was again repeated, and the filtrate was then half saturated with ammonium sulphate. A white flocky precipitate formed; the whole was centrifuged and the precipitate, the globulin fraction, was dissolved in a minimal amount of water. The supernatant fluid was completely saturated with ammonium sulphate, and the precipitate, the albumin fraction, was redissolved in a minimal amount of water. Both the globulin and albumin fractions were dialysed in collodion sacs until no more ammonium sulphate was present.

We are indebted to Dr. D. N. Nabarro, director of the pathological department at the Hospital for Sick Children, for his help and encouragement in these researches. Our thanks are also due to Dr. C. R. G. Barrington and the nursing staff at West Wickham for their valuable assistance, and to Mr. G. W. Cecil for his technical aid.

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BIRMINGHAM GENERAL HOSPITAL.—A further financial improvement is to be noted in the report of this hospital. The contributory association has increased, and not only has ordinary expenditure been met out of ordinary income, but a large proportion of extraordinary expenditure has also been provided from the same source. Substantial legacies have made it possible further to increase the reserves. The income was £86,482, as against £82,026 in the previous year, and the number of in-patients was 8369 (an increase of 63 on last year). The total number of new out-patients was 59,400, as against 56,459 in 1933.

CLINICAL TRIALS WITH A NEW ANTITYPHOID SERUM

BY C. J. McSWEENEY, M.D. N.U.I., M.R.C.P. Irel., D.P.H.

MEDICAL SUPERINTENDENT, CORK STREET HOSPITAL, DUBLIN

IN September, 1934, a new antityphoid serum was obtained from Dr. Felix, of the Lister Institute, London, for experimental purposes. The serum was unconcentrated and contained antibodies to both the "O" and the "Vi" antigens to a titre of 1 in 40,000 and 1 in 400, respectively. It was decided to give this serum to every other case admitted, alternate cases receiving equivalent amounts of normal horse serum. This plan was adhered to for the first 8 cases, but when the beneficial effects of antityphoid serum were observed, it became difficult to withhold it from subsequent severe cases. Consequently the experimental group, to date, comprises 8 cases, whereas the control group numbers only 4. Of the 8 patients receiving antityphoid serum all except one recovered, the exception being a case who perforated some days after receiving 10 c.cm., a dose we now know to have been far too small. One of the 4 controls also died, another developed a carditis which prolonged convalescence, and two children who had mild illness pursued a normal course towards recovery, though one continued to have liquid motions for six weeks from onset.

Before summarising the main points of interest in the individual cases comprising this small series, it should be mentioned that every case of proved infection with *B. typhosus* admitted to hospital since last September was either given antityphoid serum or used as a control. The intramuscular route was used except in Case 9, when some of the serum was given intrathecally. None of the 12 patients had received T.A.B. vaccine or had suffered from a previous enteric infection. The controls were actually alternate cases and were not selected. The cases here referred to were treated independently of the Palestine experiment,[1] Dr. Felix deliberately withholding his findings so that the serum might be investigated without any preconceived ideas as to its effects.

In the following notes the expression "clinically definite" means that the patient had many or all of the classical symptoms and signs of enteric infection—viz., insidious onset; steadily rising temperature in the first week, remaining remittent later, and subsiding by lysis; disproportionately slow pulse; headache (giving way later to delirium); epistaxis; bronchitis; tumid and perhaps tender abdomen; some abnormality of the digestive system, usually diarrhœa; enlargement of the spleen; rose spots; and the appearance of the diazo reaction in the urine between the 8th and 12th day of the fever. Toxæmia was graded according to severity by a system of pluses. Toxæmia graded "+" corresponds to that met with towards the end of the first week of the disease in an average case, the grading "++" indicates a degree similar to that experienced during the "stage of advance" in the average case, whereas "+++" connotes a degree equivalent to that found quite early in the very severe cases, or more commonly, in the "typhoid state" into which the average case may drift towards the end of the third week.

It is unfortunate that there is no precise method of

assessing, and of graphing, toxæmia, for the effect of the serum in reducing it was much more striking than is apparent from a study of the temperature charts, some of which are reproduced below.

CASE RECORDS

CASE 1.—John A., aged 17½ years, admitted on 8th day of disease. Clinically a definite enteric infection; Widal

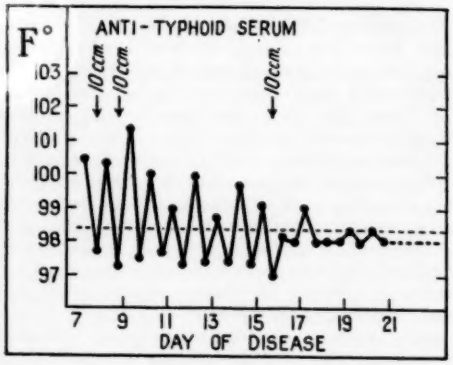

FIG. 1 (Case 3).

positive on 9th day. One of three members of the same family treated. Was first case in series to receive antityphoid serum, a single dose of 10 c.cm. being given on 17th day. Toxæmia graded "++" before serum administered. Noted as "brighter, toxæmia less" on succeeding days, but perforation suddenly occurred on 20th day. Laparotomy immediately performed revealed a large rent in the distal end of his small intestine which was sutured. Several other impending perforations in adjacent bowel noted. Patient died seven hours after operation.

Comment.—Dosage of serum far too low. This was due to Dr. Felix's absence in Palestine, his advice as to dosage not being received until some weeks later, by which time we had ourselves increased it. If such a case had come under treatment in November, three doses, each of 50 c.cm., would have been given, and in the event of perforation supervening 80–100 c.cm. would have been injected into the peritoneum before closure of the laparotomy wound. This was the only fatality among the cases receiving antityphoid serum.

CASE 2.—A control. Michael A., aged 5 years, brother of John A. (Case 1), admitted in 12th day of disease. Clinically definite but, as is usual with children, a mild case. Widal positive for *B. typhosus* 14th day. Given one injection of normal horse serum (10 c.cm.) on 22nd day, on which day motions were normal. Toxæmia was noted as absent before horse serum given. Pulse-rate kept over 100 until 32nd day of disease.

CASE 3.—Mrs. A., aged 45, mother of the two previous patients, admitted on 7th day of disease. Clinically an enteric infection. *B. typhosus* grown from the blood. Toxæmia on admission graded "++." After two doses of serum (each 10 c.cm.) given on 8th and 9th day, pyrexia at a lower level, and toxæmia "+" (Fig. 1). Final dose of 10 c.cm. of antityphoid serum on 16th day seemed to abort the disease, toxæmia being noted as absent within next 24 hours. Motions normal on 23rd day.

Comment.—This woman was quite as ill on admission as her son who died after perforation.

CASE 4.—A control. Bridget B., aged 25, admitted on 8th day of disease. Clinically definite. Widal, at first negative, was positive on 13th day for *B. typhosus*. Given 10 c.cm. of normal horse serum on 14th day. Temperature seemed to settle 48 hours later (16th day of disease) but convalescence was slow, and a carditis supervened which persisted for six weeks, the sedimentation-rate of the red cells being still slightly above normal at this late date. Motions were normal 13 days after the injection of horse serum (27th day of disease).

Comment.—This was a mild case of enteric and toxæmia was noted as absent before the patient received horse serum.

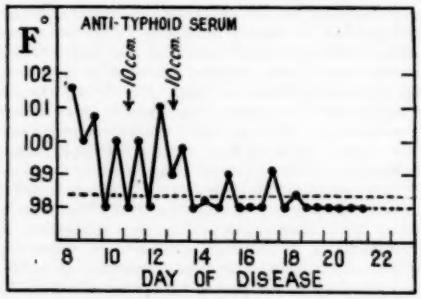

FIG. 2 (Case 5).

CASE 5. Mrs. C., aged 29, admitted on 8th day of her disease. Clinically a definite enteric, the rose spots being particularly profuse. Widal positive for *B. typhosus*, a blood culture being negative earlier. Given two injections (each 10 c.cm.) of antityphoid serum on 11th and 13th day, after which the disease seemed to abort (Fig. 2), although the motions were not normal until 31st day. On admission toxæmia graded as "+," but within 48 hours after second dose of serum the note was "toxæmia absent."

CASE 6.—A control. Elizabeth D., aged 23, admitted on 25th day of disease. Clinically an enteric infection. Widal positive for *B. typhosus* in very high titre. Given two doses (each 10 c.cm.) normal horse serum on 26th

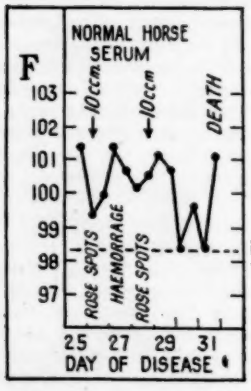

FIG. 3 (Case 6).—Control.

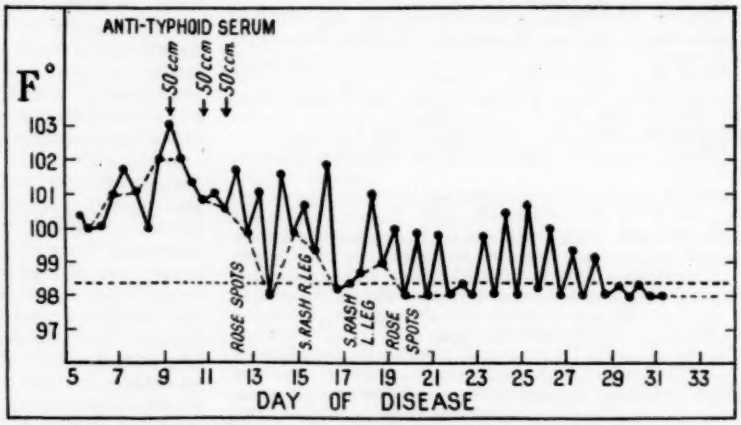

FIG. 4 (Case 7).—S. rash = serum rash. An interrupted line shows the course of the morning temperatures up to the time when they became consistently subnormal.

and 28th day. Hæmorrhage from the bowel occurred on 27th day. This was checked but patient gradually drifted into the typhoid state and died on 31st day (Fig. 3). Toxæmia on admission "++" became "+++" 48 hours after first dose of normal horse serum.

CASE 7.—Josephine D., aged 21 years, sister of Case 6. Admitted on 5th day of disease. Clinically definite. *B. typhosus* grown from blood during first week. Temperature steadily ingravescent from 100–103° F. for first five days after admission (Fig. 4), pulse-rate varying from 80–90. Toxæmia "+" on admission, "++" on 9th day of illness, when patient received first dose of antityphoid serum (50 c.cm.). Temperature curve immediately became defervescent, the morning temperature being progressively lower on next four days, reaching 98° on 14th day of disease. Same dose (50 c.cm.) serum repeated on 11th and 12th day of illness. With the exception of two pyrexial "mounds" occurring between the 14th and 20th day of disease, the morning temperature remained normal thereafter, the pulse-rate meanwhile fluctuating between 72 and 80. The two mounds in the morning temperature curve (indicated by interrupted line on chart) were definitely related to serum rashes, which—after 150 c.cm. of unconcentrated serum—were to be expected. Motions normal on 23rd day. Toxæmia graded as "+" on day serum treatment started, as "++" on days when second and third doses administered, and as "absent" two days after the last dose given (14th day of disease). The pyrexia occurring during serum rashes was unassociated with anything other than local discomfort. Rose spots continued to appear until the day before the morning temperature finally settled (19th day).

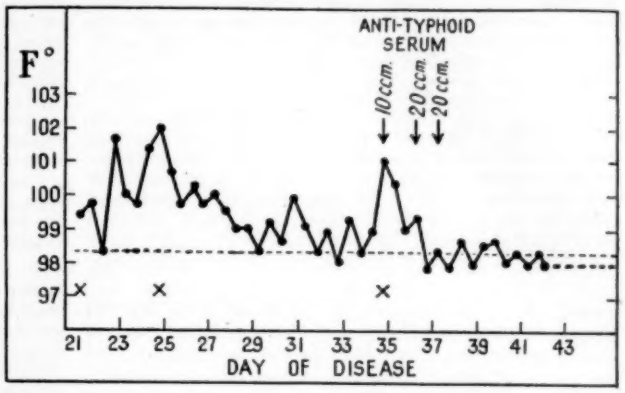

FIG. 5 (Case 9).— × = lumbar puncture.

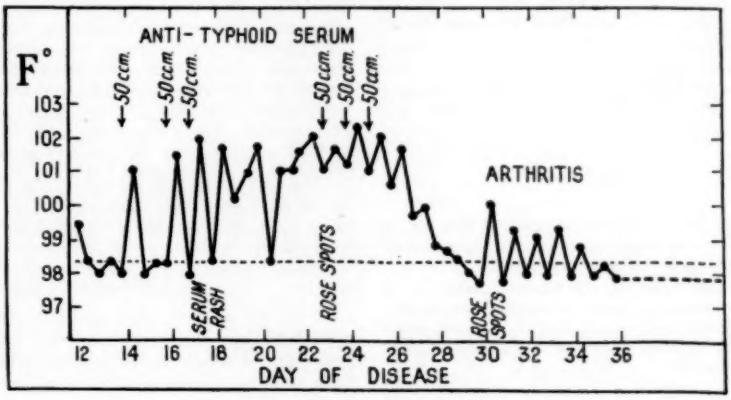

FIG. 6 (Case 10).

Comment.—In this case antityphoid serum seemed to cancel the toxæmia, and to bring the disease to a premature conclusion when the "stage of advance" should normally have occurred.

CASE 8.—A control. Annie D., aged 9 (sister of Cases 6 and 7), admitted on 14th day of disease. Clinically a mild enteric, confirmed by positive blood culture for *B. typhosus* and, later, a Widal. Given three doses (each 50 c.cm.) of normal horse serum. Toxæmia graded as "+" before serum administered, and "absent" on the day on which the last dose was given (25th day). Motions not normal until 41st day of disease.

Comment.—In this mild case the morning temperature was normal only once in the third week of the disease, whereas in the case of her sister Josephine (whose ingravescent period had presaged a severe attack) the morning temperature was normal during the same period 4 days out of 7. The toxæmia in the case of the younger child was graded as "+" during this period, whereas with Josephine it was noted as absent. The horse serum in the case of Annie did not seem to accelerate or retard the normal progress of her mild infection towards recovery.

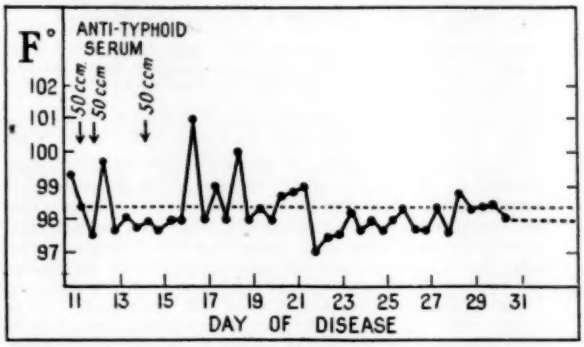

FIG. 7 (Case 11).

CASE 9.—Mary E., aged 4 years, admitted on 21st day of disease. Child extremely emaciated and presented clinical signs of meningitis which was originally thought to be tuberculous, this suspicion being strengthened when a clear fluid under pressure was obtained by spinal puncture. No tubercle bacilli were isolated from the cerebro-spinal fluid. There were no intestinal symptoms at any time. Spinal puncture repeated 4 days later with similar result—viz., clear fluid under pressure, no tubercle bacilli isolated. Patient now in critical condition, extremely wasted, very irritable, semi-comatose with occasional screaming fits which rendered segregation in a cubicle necessary. A week after the second spinal puncture, the hospital pathologist (Dr. J. H. Pollock) succeeded in isolating an actively motile bacillus from the cerebro-spinal fluid. This "organism was strongly agglutinated by typhoid agglutinating serum, less strongly by Para B serum, and not at all by Para A." The organism gave the typical black colonies on Blair and Wilson's selective medium. A similar motile organism was isolated from an

otorrhœa which had developed subsequent to admission. Accordingly, on 35th day of disease, when the temperature was 101° F. and the child apparently moribund, a third spinal puncture was performed and, after clear fluid had been withdrawn, 10 c.cm. of antityphoid serum was administered intrathecally, a dose of 20 c.cm. of the same serum was given intramuscularly on the two succeeding days (Fig. 5). The result was more dramatic than would appear from a study of the temperature charts, although the speedy diminution in pyrexia was itself remarkable. The child became rational, quiet, and proceeded to put on weight rapidly. A week later the case note was "rational now—not irritable." The signs of meningitis cleared, and the patient left hospital men-

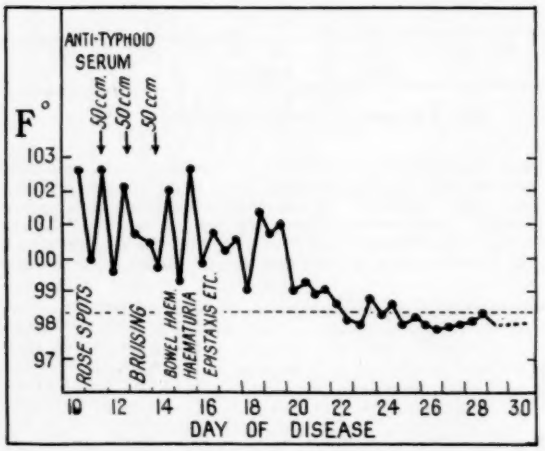

FIG. 8 (Case 12).—Hæm. = hæmorrhage.

tally and physically normal. Blood submitted for a Widal reaction on the day before serum therapy begun returned weakly positive for *B. typhosus* "*O*."

Comment.—This case appears to be an instance of primary typhoid meningitis, and a very remarkable amelioration of symptoms and signs, and of pyrexia, with a speedy and complete recovery followed the administration of antityphoid serum.

CASE 10.—Nurse F., aged 26, admitted from another hospital on 12th day of disease. Clinically a definite enteric. Blood culture negative for *B. typhosus* on 12th and 21st day but Widal strongly positive for that organism on 14th day. *B. typhosus* later isolated from urine. Received three doses (each 50 c.cm.) of antityphoid serum on 14th, 16th, and 17th day of disease. Temperature did not settle thereafter, a generalised urticarial serum rash appearing on 18th day (Fig. 6). The return of liquid motions, increase in size of spleen, the appearance of rose spots, return of the diazo reaction in the urine, and a rising temperature after the serum rash had faded suggested the onset of a relapse. Serum was repeated on 23rd, 24th, and 25th day of disease, 50 c.cm. being given on each occasion. Two days after the first dose of the second series of injections the temperature will be noted to have taken a downward trend and, apart from a mild attack of arthritis causing local discomfort, convalescence was speedy and complete. This patient never complained after her first serum treatment except about her serum rash and arthritis. The latter was undoubtedly a serum phenomenon, as the patient had in all 300 c.cm. of natural serum, double the maximum dose given to any other case. Motions were normal on 33rd day. Rose spots continued to appear until 30th day.

Toxæmia in this case graded as "++" on admission and "absent" immediately after first series of injections had been completed.

CASE 11.—Frank G., aged 54, a bedridden paralytic, admitted on 11th day of disease, much wasted and with extensive bedsores. Clinically a definite enteric, blood culture positive for *B. typhosus*, also Widal and later fæces. On admission toxæmia "++." Given antityphoid serum (3 doses, each 50 c.cm.) on 11th, 12th, and 15th day of disease (Fig. 7). Subsequent toxæmia difficult to assess because of concurrent paralytic and mental condition. Appeared much better from 18th day, temperature remaining settled after 22nd day though motions not normal until 37th day.

Comment.—The clinical impression is that had this man not been given antityphoid serum, he would not, in his lowered state of vitality, have survived his attack of enteric.

CASE 12.—Kathleen H., aged 17. Admitted on 10th day of her disease. Clinically a definite enteric. Blood culture and Widal positive for *B. typhosus*. Toxæmia "++" on admission, quickly becoming "+++" on development of hæmorrhages from mucous membranes of nose, mouth, intestine, and bladder. Large areas of subcutaneous hæmorrhage with petechiæ, hæmorrhage into rose spots, and discrete subconjunctival hæmorrhages also occurred. In addition, extravasation took place into the skin of the abdomen, which had been blistered by poulticing before admission. Patient's condition was now very critical and the typhoid state seemed imminent. Antityphoid serum was given in 3 doses of 50 c.cm. on 11th, 12th, and 13th days respectively (Fig. 8). Within 4 days of the last dose her condition showed a remarkable improvement. Toxæmia was definitely less (++), the patient was again rational, hearing less blunted, and all restlessness gone. The urine which had contained a large quantity of blood for several days was clear on 19th day of disease, on which day the toxæmia was noted as absent. Stools were free of blood on 18th day. The temperature was normal on 22nd day, and remained so thereafter. Motions were formed on 26th day.

Comment.—The beneficial effects following serum therapy in this case were the most striking observed in the series of cases under review. Hæmorrhagic typhoid is a very rare disease (E. W. Goodall [2] says he saw only one in his extensive experience, while the late C. B. Kerr [3] refers to it as "fortunately most uncommon" and "very fatal").

CONCLUSION

It is, of course, not claimed that any sweeping assertions can be made for the efficacy of this new antityphoid serum on so small a series of observations. This is more especially the case as the controls were, on the whole, not good. It is however possible to say that out of 8 cases receiving antityphoid serum, 7 ceased to cause anxiety within a few days of the last dose, and the only failure was the case receiving a very inadequate single dose who died from a local complication—viz., perforation.

I have to acknowledge the great kindness of Prof. J. W. Bigger who elected to carry out the bacteriological work in connexion with this investigation. I must also express my indebtedness to Dr. F. N. Elcock (senior resident medical officer at Cork-street Hospital) for his careful day-to-day notes on the series of cases here reviewed.

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HOSPITAL TREATMENT FOR UNEMPLOYED.—Lord Derby, as president of the Merseyside Hospitals Committee, has given his support to a new scheme for the provision of voluntary hospital care for unemployed families. This scheme is known as the Friends of the Sick Poor, and a condition of membership is an undertaking to adopt an unemployed family for voluntary hospital care at an annual cost of 10s. per family. It is hoped that this scheme will attract support from people who do not come within the penny-in-the-pound fund for Merseyside hospitals.

THE POSTERIOR LOBE OF THE PITUITARY GLAND

ITS RELATIONSHIP TO THE STOMACH AND TO THE BLOOD PICTURE

BY E. C. DODDS, M.V.O., D.Sc., M.D., F.R.C.P. Lond.

COURTAULD PROFESSOR OF BIOCHEMISTRY IN THE UNIVERSITY OF LONDON

G. M. HILLS, B.Sc., Oxon.*

R. L. NOBLE, M.D. Toronto †; AND

P. C. WILLIAMS, B.Sc. Lond.*

(*From the Courtauld Institute of Biochemistry, Middlesex Hospital, London*)

IT has previously been shown (Dodds, Noble, and Smith [1]; Dodds and Noble [2]) that it is possible to prepare an extract of the posterior lobe of the pituitary gland which when injected subcutaneously into animals will produce an acute hæmorrhagic lesion of the acid-bearing area of the stomach; and the animals usually recover completely in a period of some ten days. The same effects can be produced in rabbits by the oral administration of the extract. These lesions have been described in previous papers in detail. It has been shown that if the contents of the stomach be rendered alkaline prior to injection, it is impossible to obtain the characteristic reaction. The most significant points concerning the gastric lesion are, firstly, its extremely accurate limitation to the area of the stomach in which oxyntic cells are found, and, secondly, the complete absence of lesions in other parts of the alimentary canal. It has also been demonstrated that similar lesions can be produced in all the laboratory animals tested—namely, monkey, cat, rabbit, guinea-pig, rat, and mouse.

The present communication deals with the extension of these investigations, and it will be seen that the extract exerts a profound influence upon the blood picture.

PRODUCTION OF CHRONIC ULCERS

In view of the acute lesions produced by a single injection, it was decided to study the effects of repeated doses of the extract. A typical experiment was as follows: a rabbit was given 40 c.cm. of standard B.P. pituitrin by stomach-tube every 7 days over a period of 8 weeks. During this time the animals appeared to be in good condition and did not exhibit any unusual symptoms after the initial injection. At autopsy a typical punched-out ulcer was found on the greater curvature which had perforated but was healed by omentum. Chronic ulcers have been produced following a single subcutaneous dose of 75 mg. per kg. of the acetone picric acid extract of the posterior lobe of the pituitary. An ulcer has also been found following four subcutaneous injections of 5 c.cm. of standard B.P. pituitary extract, given every other day. These ulcers are always single and situated in the acid-bearing area of the stomach. Their gross appearance is typically that seen in chronic gastric ulcers in man. We believe that this is the first occasion on which chronic gastric ulcers have been produced with any regularity in animals by the injection of an extract of a normal tissue.

EFFECT ON GASTRIC SECRETION

An attempt was made to study the mechanism for the production of the lesion. Since it has been shown that the rendering of the stomach contents alkaline is capable of abolishing the typical lesion, it follows that gastric acidity must in some way be associated with this phenomenon. A technique for studying the reaction of rabbits' stomachs to histamine was worked out. The following is a very brief account of a typical experiment. The rabbits were put on a milk and bran diet for two weeks to allow the stomach contents to become sufficiently liquid to be washed out. Under sodium amytal anæsthesia the pylorus was ligatured, the most dependent portion of the stomach opened, and an external fistula was established. Through this the contents were removed and the stomach was washed out. In the control series of animals the resting juice was collected for half an hour. This was followed by the subcutaneous injection of 0·25 mg. per kg. of histamine. Thirty-minute specimens were collected, and were titrated for free hydrochloric acid and for total acidity. In the experimental group the above technique was followed except that these animals received 2 c.cm. per kg. of standard B.P. pituitrin intravenously, and then after 30 minutes the histamine injection. The control series showed a typical profuse secretion due to the histamine with the free HCl reaching a peak of 80–130 c.cm. of N/10 HCl per 100 c.cm. of juice in 90–120 minutes. In the experimental group we have never found any free HCl secreted, even though large doses of histamine have been repeated at the end of 5 hours. This reaction has also been obtained using the acetone picric acid extract administered intravenously. From these and other experiments it would appear that injection of the extract is capable of causing a temporary inhibition of secretion of hydrochloric acid, in such a way that the stomach will not react to the histamine stimulus for a period of some 6 hours. It is interesting to note at this juncture that other previous workers have called attention to the fact that injection of pituitary extract reduced gastric acidity.[3 4]

EFFECTS ON BLOOD

It has been shown [5] that very profound changes occur in the blood of animals injected with this extract. Thus, if a rabbit be injected subcutaneously with the preparation, it will be found on the fifth day that a severe anæmia has developed, the blood count being reduced from 6,000,000 down to as low as just over 1,000,000 red cells. The hæmoglobin is also reduced but not proportionately to the same extent. On the fifth or sixth day a reticulocytosis appears which may rise to as high as 50 per cent. There is a marked anisocytosis and a definite macrocytosis. If the animals be killed obvious changes are seen in the spleen, such as hæmorrhagic infarction, and there is evidence of a stimulation of the blood-destroying system. The intestines are full of bile, and it would appear that the anæmia may possibly be ascribed to an increased blood destruction. If left alone the animals will recover completely.

DISCUSSION

It is impossible at the present time to offer any complete explanation of the various phenomena recorded, but the following remarks may assist in an attempt to estimate the significance of these investigations. In the first instance it must be

* Working with a grant from the Medical Research Council.
† Working with the Ellen Mickle Fellowship from the University of Toronto.

pointed out that the substance, or substances, responsible for this reaction are contained only in the posterior lobe of the pituitary gland. Exhaustive controls have been made with other tissues of the body, employing not only doses identical to those which prove active in the case of the pituitary, but with doses many times larger. We have, however, been unable to obtain with these any action upon the stomach or blood picture. The following is a list of tissues from which extracts have been prepared: spleen, liver, kidney, testes, muscle, pancreas, suprarenal, brain, stomach, thyroid, and placenta.

As pointed out in previous publications, the factor or factors necessary for the production of a gastric lesion and blood picture are contained in the commercial pituitary extract (B.P.) as well as in the pituitary extract made by the acetone-picric acid process by the method of Dodds and Dickens.[6] It seems at first sight that the quantity of material injected is so great as to make it doubtful whether the phenomena described are really exaggerations of a natural process. It must be borne in mind, however, that the B.P. pituitary extract is standardised for the oxytocic and vasopressive principles in units which bear no relation to the phenomena described. By application of the method of preparation and purification of the vasopressive principle described by Kamm et al.[7] it has been found that the actual weight of an effective dose of the active principle may be reduced to a figure quite compatible with those of other hormones. On the weight basis, therefore, it appears that no theoretical objection could be made to our observations on these grounds.

A full explanation of the connexion between the pituitary gland and the stomach and the blood picture can only be arrived at by a study of the hypophysectomised animal, and this is in active progress at the present time in association with Dr. A. S. Parkes and Mr. I. W. Rowlands.

From the clinical aspect, our observations might possibly provide an explanation for a number of hitherto puzzling phenomena. For example, in Simmonds's disease it is known that there is atrophy of the organs of the reticulo-endothelial system.[8,9] Again, in certain cases of basophil adenoma of the anterior lobe of the pituitary gland, ulceration of the stomach[10] and also erythræmia have been recorded.[11] In cases of duodenal ulcer polycythæmia has also been observed.[12] The occurrence of acute gastric lesions following operations on the base of the brain has been recorded on several occasions in the publications of Harvey Cushing.[13] From these investigations it seems justifiable to consider the possibility of a hormonal connexion between the posterior lobe of the pituitary gland, the stomach, and the blood picture.

One of us (E. C. D.) is indebted to the Medical Research Council for a grant towards the defrayment of the cost of material for this investigation.

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CLINICAL AND LABORATORY NOTES

PARALYTIC ILEUS CURED WITH PROSTIGMIN

BY W. E. DAVID, M.C., M.B. Sydney

A REPORT to the Therapeutic Trials Committee of the Medical Research Council published a year ago[1] described the use of prostigmin in a series of cases of abdominal distension following operation. The dose ranged from 1·0 to 4·0 c.cm., but the larger quantity was used on one occasion only and the usual practice was to give 1·0 c.cm., repeated if necessary. None of the patients mentioned in that report seem to have been as gravely ill as the one who is the subject of the present note. The case is interesting not only because almost every known remedy (except acetylcholine) was previously given, but because the dose of prostigmin administered was the large one recommended by Dr. M. B. Walker for the treatment of myasthenia gravis.

A. B., aged 23, was seen on March 30th, 1935, with acute appendicitis. Temp. 101°F; pulse-rate 88. He had had abdominal pain for 48 hours before sending for medical assistance. The operation revealed a gangrenous appendix, which was removed and a drainage-tube inserted. On the following day the tube was changed and the patient was given a turpentine enema, with a very small fæcal result. On April 2nd, at noon, 2 drachms of Cascara Evacuans were given. This was vomited and the dose repeated at 2 P.M. He vomited at 7.30 P.M. and was complaining of abdominal pain and distension. No result from aperient was obtained, so he was given two vegetable laxative tablets at 8 P.M.

He vomited off and on the whole night; the abdomen remained distended and there was no result (either flatus or fæces) from the aperient. Hourly foments were applied to the abdomen and on April 3rd a turpentine enema produced a good fæcal result and he was put on to 1 c.cm. pituitrin, to be followed by 0·5 c.cm. three-hourly. Towards noon his distension had increased and he was unable to pass flatus alone or with the help of a flatus tube. Hiccup began and his distension increased. Nothing abnormal could be felt per rectum. Towards midnight he was given another turpentine enema, which gave a good, formed result, but the abdomen still remained tensely distended and the skin was stretched and shining, and the patient looked drawn, haggard, and altogether extremely ill, although his pulse and temperature did not appear to reflect the severity of his abdominal condition. He was at 12.40 A.M. on April 4th put on to eserine, gr. 1/100 every four hours.

He vomited green bile-stained fluid and hiccupped off and on the whole day. The abdomen at 4.30 P.M. was even more distended and no gurgling could be heard with the stethoscope. A turpentine enema gave a fluid return with streaks of blood-stained mucus, but no flatus was passed. An ox-gall enema was given at 6.20 P.M. with no result, followed at 9.30 P.M. by 20 c.cm. of anti-gas gangrene serum. An hour later the patient was given a spinal anæsthetic (Stovaine) with no result. At midnight he was given an enema of milk and molasses with no result. He was still vomiting and had a very bad night; his temperature on April 5th was 100°, the pulse-rate varying

[1] Carmichael, E. A., Fraser, F. R., McKelvey, D., and Wilkie, D. P. D.: THE LANCET, 1934, i., 942.

between 90 and 112. He had been having salines subcutaneously and saline and glucose per rectum for the preceding 48 hours, and this was continued throughout the day, and hot fomentations and radiant heat were applied to the abdomen.

At 7.35 P.M. he was given 5 c.cm. of prostigmin subcutaneously. Five minutes after the injection gurgling could be heard in the abdomen and in ten minutes he passed a large action followed by a large quantity of flatus, and his bowels continued to act for 40 minutes. His condition was much improved on the following day, but the abdomen was still somewhat distended despite frequent motions. The effect of 1 c.cm. of prostigmin was tried, but this did not seem to affect the condition in that dosage. The stomach was washed out with saline and half a pint of saline left in. This was repeated twice during the day, and by the evening his vomiting, which had been aggravated by a shortage of chlorides, ceased.

Dr. Walker in the treatment of myasthenia gravis recommends that atropine, gr. 1/100, should be given with the 5 c.cm. of prostigmin, to counteract any slowing of the heart's action and the intestinal peristalsis which ensues. This, of course, was not given in this case, but the pulse was carefully watched and did not vary much as a result of the injection. The point to be stressed is the dosage of prostigmin, and there appears to be little doubt, if one can judge from one apparently hopeless case, that it should be given a trial before other methods as soon as the diagnosis of paralytic ileus has been made.

The cause of paralytic ileus is obscure, but apart from toxæmia there is probably a nervous factor. Anxiety at the thought of an operation may cause over-action of the sympathetic, which is known to have an inhibitory effect on intestinal peristalsis, while a local lesion of the peritoneum or perhaps the gut may cause reflex inhibition of peristalsis. Prostigmin may be presumed to act by antagonising inhibition of both kinds.

CLOSURE OF LARGE POSTAURICULAR FISTULAS AND DEPRESSIONS

By G. W. Dawson, F.R.C.S. Irel.
CONSULTING SURGEON TO THE GOLDEN-SQUARE HOSPITAL FOR DISEASES OF THROAT, NOSE, AND EAR, LONDON

SMALL postauricular openings are easily closed. Occasionally, however, one is confronted with cases in which much substance has been lost and an unsightly cavity is left behind the ear with a fistula leading to the additus. The following case illustrates my method of filling such cavities. Mrs. A, aged 30, whilst on holiday in August, 1933, contracted influenza and double acute mastoiditis. An extensive Schwartze operation was performed on each mastoid, and when she was seen by me some months later there was a large depression behind each ear measuring 1¼ in. vertically and 1⅛ in. horizontally with some necrosis at lower edge of each cavity (Fig. 1, C). In one ear there was a fistula leading down to the additus.

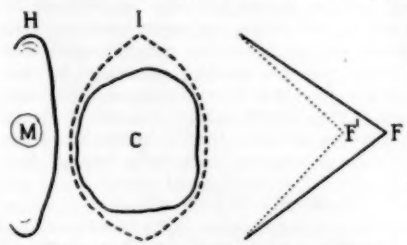

FIG. 1.—The cavity (C) and the incisions (I. and F). H = helix. M = meatus.

An incision (I) was made round the edge of the cavity and the diseased bone was removed. The posterior bony wall of the meatus (M) was lowered and the margins of the bony cavity were well bevelled. A V-shaped incision (F) was then made well behind the cavity, and the entire thickness of the flap was separated from the cranium and displaced forwards. This made it possible to stitch the edges of the incision (I) without any tension, the result being shown in Fig. 2. One side healed by first intention; the other, in which there was a fistula, continued to suppurate through the meatus for a few weeks. The incisions made to form the flap are within the hair margin, heal by first intention, and are invisible. This operation can be combined with a temporal muscle graft.

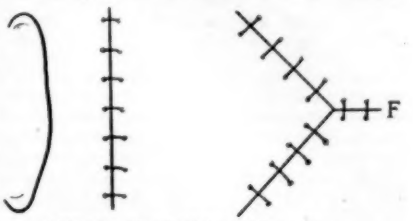

FIG. 2.—The incisions after closure.

POSTURAL HYPOTENSION WITH TACHYCARDIA

By T. A. Hughes, M.D. Dub., F.R.C.P. Lond.
LIEUT.-COLONEL, I.M.S.; PHYSICIAN, MAYO HOSPITAL, LAHORE; AND
Mohammad Yusaf, M.D.
CLINICAL ASSISTANT AT THE HOSPITAL

A CASE of postural hypotension has recently been described by Croll and Duthie[1] who give some particulars of previously recorded cases, numbering 18 in all. The chief feature of their case was a fall in the systolic and diastolic pressures, accompanied by giddiness, when the patient changed from the supine to the sitting and from the sitting to the standing position. The fall was associated with a great decrease in the output of water by the kidneys. It was not prevented by abdominal compression, by the application of tourniquets round the limbs, or by the administration of adrenaline, pituitrin, and histamine. The pulse-rate is stated to have showed "a normal response to change in posture—namely, an increase in pulse-rate in the erect position and a decrease in the recumbent." The variation in rate is not given but it was presumably similar to that noticed in normal subjects by Tait McKenzie (whom they quote)—namely, a difference of about seven beats per minute between the lying and the standing positions. Among the other cases referred to by Croll and Duthie is one described by Sanders[2] in which tachycardia and abnormal changes in the electrocardiogram accompanied the fall in blood pressure brought about by change of posture. Indefinite changes in the nervous system were present in three cases described by Bradbury and Eggleston.[3] In Croll and Duthie's patient both knee-jerks were absent and there was a pseudo Argyll Robertson reflex in the left pupil.

Our own patient was a Hindu male, aged 28, a lorry driver, who was admitted to the Mayo Hospital, Lahore, on May 26th, 1933, complaining of attacks of palpitation and giddiness associated with a good deal of mental discomfort and difficulty in breathing, loss of appetite, heaviness in the epigastrium after meals, and pain in the lower part of the chest.

He had been married for five years and had two children, aged 3½ years and 8 months, both healthy. He was a

vegetarian. According to his statement he had been taking opium (amount unknown) for three years but had given it up two months before admission to hospital. There was no history of previous illness other than probable malaria.

History of present illness.—The patient stated that attacks of palpitation and giddiness began about a year before admission and were often accompanied by a sensation of nausea. The attacks ceased when he lay down, but he also found that relief was obtained from walking about. He never fainted and was able to carry on his work. The palpitation and giddiness got no worse during the year, but he became considerably weaker and the pain in the chest rather increased. There was no cough and no loss of sexual power. The temperature occasionally rose to 99° F.

Physical examination.—The patient was 5 ft. 6½ in. in height and of spare build. Nothing abnormal was detected in the heart and lungs by ordinary and X ray examination. The electrocardiogram was normal. The abdomen was somewhat tender and resistant in both iliac fossæ. Skiagraphy showed a spastic colon with stasis. The nervous, genito-urinary, and hæmopoietic systems appeared normal. The teeth and throat were healthy.

The attacks of giddiness, which were related to changes from the horizontal to the erect posture, were associated with a marked increase in the pulse-rate and a less marked fall in the systolic blood pressure. The diastolic pressure was low even in the supine position and altered little with change of posture. Further, the fall in systolic pressure when the patient sat up from the recumbent position was increased very little or not at all on standing, provided he remained sitting for a couple of minutes or so. The pulse-rate, however, was always much more frequent in the standing than in the sitting position. Typical figures were :—

	Recumbent.	Sitting.	Standing.
Blood pressure ..	.. 110/55	86/55	86/50
Pulse-rate per minute ..	70	92	125

As in Croll and Duthie's case the blood pressure in the supine position varied from time to time. The readings sometimes went up to 130/70 or thereabouts, the pulse pressure being always relatively high. There was no evidence of aortic incompetence. An injection of 1 c.cm. of adrenaline did not alter the circulatory reaction to changes of posture. The effects of pituitrin, histamine, tourniquets, and abdominal compression were not tried.

A prominent feature of the case was the pronounced tachycardia which seemed to be compensatory for the fall in systolic pressure. This compensation took a little while to adjust itself. When a direct change was made from the supine to the standing position the pulse-rate did not reach a maximum for about two minutes. The increase in heart-rate was brought about through the normal reflex mechanisms. The electrocardiogram showed that a sinus rhythm was maintained in the erect as well as in the horizontal position. With rapid rates the P and R waves coalesced but there was no other change. The low diastolic pressure in the absence of any leak from the arterial system indicated defective vascular tone. The carotid sinus reflex could be easily elicited, a prompt fall in pulse-rate being produced by pressure on either sinus. It is generally stated that compensation for the hydrostatic effects of gravity on the circulation is brought about through the buffer action of the carotid sinus and the aortic nerves. MacWilliam,[4] however, is of opinion that this mechanism acts only in the horizontal position and that compensation in the erect posture is effected through reflexes from some part of the vascular circuit in the lower limbs. Our patient's statement that his "attacks" were relieved by walking about is of interest in this connexion. MacWilliam found that in Croll and Duthie's patient movements of the lower limbs in the erect posture prevented a fall of pressure or even brought about a rise.

The underlying cause of the defect could not be determined. The observed facts indicate that the fault lay chiefly in the effector mechanism of the postural vasomotor reflex. There was no reason to suspect serious derangement of the receptors, nor was there any evidence of disease of the central nervous system. The patient's abdominal symptoms and signs, together with occasional fever, led to a suspicion of abdominal tuberculosis which is fairly common in adult Punjabis. Such a condition might interfere with the action of the splanchnic vasoconstrictor mechanism.

SUMMARY

A case of postural hypotension associated with sinus tachycardia is described in a man aged 28. The cardiovascular system was otherwise normal. It is considered that the tachycardia was compensatory for defective vasomotor control in the erect posture.

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MEDICAL SOCIETIES

ROYAL SOCIETY OF MEDICINE

SECTION OF THERAPEUTICS AND PHARMACOLOGY

A MEETING of this section was held on April 30th with Dr. GEORGE GRAHAM in the chair.

Dr. C. A. NEYMANN (Chicago) read a paper on the

Treatment of Disease by Electropyrexia

He traced the history of treatment by fever and observed that some of the earliest pyrexial-producing agents were only in degree more radical than some of the most modern. Fever alone was the important common factor in all methods. The death-rate with malaria treatment of general paralysis ranged between 10 and 20 per cent. and improvement was but slight. Diathermy compared very favourably, showing a 2·5 per cent. death-rate, 34 per cent. improved, and 29 per cent. complete remission. The personal factor accounted for variations in results from different centres; if demented patients were treated with few pyrexial attacks and low temperatures the results would naturally be less good. In private practice Dr. Neymann had had a recovery-rate of 8 per cent. after at least 20 treatments with a pyrexia of 103°–106° F. maintained for 11–14 hours. The death-rate had been negligible—only 1 death in all. The serological changes did not correspond with the clinical benefit, though improvement was noted in some respects. The cerebro-spinal Wassermann reaction was very slow to change, even in patients who had returned to work. Only 2 of 18 patients followed up had failed to continue at work. Diathermy therefore offered a hope of recovery to every early case, but the grandiose type had a better chance than the depressed and slowly dementing. A comparison of three groups of 50 patients treated with sodoku, malaria, and diathermy showed the great superiority of the last method. A

single intense bout of fever could not cure when the organisms had adapted themselves to their habitat over years and were heat-resistant from the start.

Tabes was also favourably influenced, and progress could be judged by the arrest of crises and lancinating pains; the benefit was so great and immediate as to be almost unbelievable. Cerebro-spinal fluid and blood changes accompanied the clinical improvement. Several workers had treated the rarer cerebro-spinal syphilis; resistant cases were suitable for pyrexial treatment and often responded excellently. The benefit was partly due to destruction of the treponema and partly to the vasodilatation. Syphilitic optic atrophy, treated with intensive pyrexia, up to 107·6° F. for part of the time, had shown some promise: 4 of 7 patients treated had retained the vision they had.

Two male patients with primary chancres had been treated: 1 had recovered and the other had developed secondary symptoms. The urethral temperature was 1° higher than the rectal, and presumably therefore at least 106° was required. One patient so treated had lost his primary lesion, but had developed modified secondaries wherever his skin had been uncovered (and presumably therefore cooled) during treatment. Therefore the more recent patients had been intensively treated in special cabinets, and thermocouples in cisterna magna, rectum, axilla, and under the skin were used to control the temperature throughout the body. External and internal temperatures were kept well above 105° F. Nevertheless, secondaries had appeared, although the chancres healed promptly and were free from organisms. After one treatment the treponema could be seen breaking up and taking on a coccal appearance. Hyperpyrexia therefore could not eradicate the virus, though it influenced and partially arrested the progress of the disease. Work was in progress to find out whether arsenical treatment as an adjuvant was best given during or after the pyrexia.

Four patients with a parkinsonian syndrome had also shown benefit, one of them being enabled to work a typewriter. Multiple sclerosis had been treated in 25 cases. There had been lasting improvement in all mild cases and some improvement in average advanced ones. Four very advanced cases showed no improvement: 1 had died as a result of treatment and 1 soon after it. Sydenham's chorea could be treated by electro-magnetic induction and the results had been astoundingly good. The fever should not be above 104°–105° F. for children. The treatment had also proved beneficial in asthma—22 out of 44 cases showing lasting remission, and others some improvement—and in chronic arthritis. The hypertrophic type of arthritis did not react well to hyperpyrexia, but the chronic infectious type was decidedly improved. Electropyrexia was the treatment of choice in gonorrhœal arthritis. It had been used in many other conditions, but its uncritical application was apt to bring it into disrepute.

Discussion

The CHAIRMAN said that electrical methods of producing fever would remove the undesirable necessity for giving a patient one disease in order to combat another. Although both methods might cause anxiety, yet with electrical treatment the physician knew when the critical times were due. A general paralytic might be exceedingly ill and uncomfortable at noon, and perfectly well two hours after the fever was over. He hoped for good results in all cases of asthma

Dr. F. J. NATTRASS, describing the results of short-wave high-frequency currents in the treatment of 15 cases of general paralysis, said that ten or twelve treatments had been considered to be adequate. Dr. Neymann, however, had convinced physicians that this was not a sufficient number. Two of the patients had died as a result of the treatment, and two others afterwards; all had been relatively old and not very suitable cases. From what the lecturer had said, they appeared to have been treated too frequently, treatment having been given on alternate days. Working in a general hospital, he and his colleagues had used amytal and once or twice avertin anæsthesia to mitigate the distress caused by the treatment; morphine had been useless, and hyoscine had caused alarming symptoms, sweat ceasing and pyrexia being difficult to control. In 3 cases of tabes, complete relief from lightning pains had been given by the treatment, and a few cases of gonococcal arthritis had been strikingly benefited.

Dr. NEYMANN, in reply, said that excited and maniacal patients had to be strapped down. Patients with asthma, tabes, and Parkinson's syndrome had to be given relief from the effects of the pyrexia. Hyoscine was very dangerous, but morphine might be used in large doses, starting with gr. ¼, repeated in fifteen minutes if no relief were given. Some cases reacted very well to paraldehyde, but it made the patient smell offensively. Ten drachms might be tolerated without any harm, particularly as the temperature rose and the respiration-rate increased. He deprecated the indiscriminate use of artificial pyrexia in France for practically all diseases. It should, he thought, be kept for diseases to which the body reacted with a small amount of fever: more or less subacute or chronic conditions. It was probably useless in endocrine disorders and malignant disease.

Dr. W. W. PAYNE said that the type of change observed in electrical hyperthermia was complete disappearance of all the phosphate from the urine, and the fall of the inorganic phosphate content of the blood to under 2 mg. per 100 c.cm. as the temperature rose. As it fell, the phosphate rose accordingly. The creatine content followed a slightly different plan, rising and falling with the temperature. The work had all been done with children, who normally excreted creatine in the urine. This creatine would disappear at certain periods between the exposures and would return during pyrexia. The phenomenon was probably due to the breakdown of phospho-creatine in the muscles under the influence of adrenaline. It was difficult to know whether this was a response to the infection or to the fever.

Dr. AGNES SAVILL inquired whether there was any difference in the results of artificial and of natural pyrexia.

Dr. NEYMANN answered that the blood creatine decreased after a series of fever treatments, but increased at the time of each treatment. It increased, like the non-protein nitrogen and the urea nitrogen, as a concentration phenomenon, and finally rested at a lower level. Pyrexia was believed to influence the rapidity of excretion of all waste products. It had been suggested that the treatment might be of some use in chronic interstitial nephritis with nitrogen retention. The lactic acid content of the blood, which was formed from the katabolism of the muscles and of the body, increased under pyrexia. Consequently the hydrochloric acid content of the stomach had at first sight a tendency to increase, but later it decreased on account of the great excretion of salt due to sweating. It would be easy to find out the

respective effects of toxæmia and pyrexia if the curves recorded in a bout of toxic fever were reproduced afterwards electrically and physiological observations were made. In conclusion, he said that the particular method used to produce pyrexia was unimportant; it was the man who counted and not the machine. The electro-magnetic induction method heated the inside of the body but not the fat, for it heated tissues in direct proportion to the electrolyte content of the colloids; it therefore did not cause burning.

ROYAL ACADEMY OF MEDICINE IN IRELAND

A JOINT meeting of the sections of medicine and pathology was held on April 5th, with Dr. V. M. SYNGE, president of the section of medicine, in the chair.

Antityphoid Serum

Mr. A. FELIX, D.Sc. (Lister Institute, London), read a paper on experimental and clinical results with a new antityphoid serum. He described experiments from which it was concluded that the efficacy of a therapeutic antityphoid serum would depend on the presence in it of both the Vi and O antibodies. Serum of this type had been prepared from horses at the serum department of the Lister Institute and had given encouraging results in the treatment of cases of typhoid fever in Palestine. These results were described in THE LANCET of April 6th (p. 799).

Dr. C. J. MCSWEENEY reported his experiences with the serum in Dublin. They are set out in detail on p. 1095.

Dr. W. R. O'FARRELL (president of the section of pathology) expressed a hope that Dr. Felix's experiments would throw light on the question of antityphoid vaccination. Referring to the leucopenia constantly present in enteric he suggested that the leucocyte count might be helpful in assessing the immediate effects of the serum.

Prof. J. W. BIGGER said that the Vi antigen described by Dr. Felix was an entirely new conception, and offered great therapeutic possibilities, one of the chief of which was its utilisation in establishing active immunity. The treatment of infections by antibacterial sera had hitherto been very disappointing. The only antibacterial serum which he personally thought was really good was antimeningococcal serum. Here one was dealing with an anti-endotoxin. It should however be remembered that the new antityphoid serum was still in the experimental stage, and he thought it should be entrusted only to those prepared to use it in a scientific way, and in a hospital where proper bacteriological facilities existed.

Prof. W. D. O'KELLY asked how a vaccine could be prepared which would contain the Vi antigen, and if the febrile reaction to the vaccine might be neutralised by giving at the same time some serum.

Dr. T. T. O'FARRELL said it was disappointing that Dr. Felix's experiments on mice had not all come out clinically as one would have expected. In the old days many cases of typhoid cured themselves, presumably because the patients produced their own antibodies. In Dr. Felix's experiments there was an enormous number of cases which showed Vi antigen in the serum, and yet in many cases the antibody did not arrive until quite late in the course of the disease. From this one would not think the Vi antibody to be of much use in affecting the progress of a case. Referring to the use of the antiserum, he was rather surprised to hear that in the case of perforation this serum had done good. The danger of perforation was due to the *Bacillus coli* which invaded the peritoneum, and therefore he could not see how antityphoid serum could be useful in these cases.

Prof. LEONARD ABRAHAMSON drew attention to the fact that clinicians had at first used serum only in alternate cases, but after a time had felt obliged to use it in every case.

Dr. G. C. DOCKERAY said that whilst it appeared that in most cases of typhoid Vi antibodies were produced in low titre, in one case described by Dr. Felix the Vi titre was higher on the 77th day than the Vi titre of the therapeutic sera. This suggested the possibility of being able to use convalescent serum derived from patients who did develop high titres.

Dr. A. R. PARSONS pointed out that this was not the first attempt to treat typhoid with serum. In Paris in 1909 cases had been treated with Chantemesse's serum. At first this was reported to give very good results, but very little had been heard of it since. Again, Grasset's serum had been described as very useful, but little was heard of that either. Though the results presented by Dr. Felix and Dr. McSweeney were very good, not enough cases had yet been treated to reach any conclusion statistically.

Dr. R. H. MICKS suggested that Dr. McSweeney should get in touch with county medical officers of health and medical superintendents of country hospitals and ask them to send him their early cases.

Dr. J. FLOOD said that the clinical evidence so far available consisted in the cases Dr. Felix had treated in Palestine and those Dr. McSweeney had treated in Dublin. In his opinion these did not constitute a sufficient number on which to base any definite conclusions. Looking at the temperature charts, the critical period in all of them appeared to be that period at which the patient got the serum. He thought it possible that if Dr. McSweeney had had a series of cases treated with the ordinary antityphoid serum the critical period would have fallen at the same time—namely, the day on which the patient got the serum.

Dr. V. M. SYNGE (president of the section of medicine) agreed with Prof. Bigger that one should not be unduly enthusiastic about this new treatment; the results were very encouraging but the number of cases very small. There was a great deal of typhoid in Ireland, and Dr. McSweeney should have plenty of material to work on.

Dr. FELIX, in replying, said he had been cautious in not drawing any statistical conclusions; to do so would be quite wrong. He was quite aware of the older sera which had been prepared, tested, and abandoned, and was sure that Chantemesse's serum must have been good. It was the only one in whose preparation live organisms had been used. All the sera which were now being produced were produced in a way which destroyed the antibody. It was impossible to compare the in-vitro titres in relation to their protective action. Caution and scepticism were perfectly sound in relation to his serum, which was still in the experimental stage. His purpose in Palestine was to establish whether there was anything to parallel the clear-cut results obtained in animals. He personally would not expect serum to clear up a local complication like a perforation.

Dr. MCSWEENEY said he would be very glad to extend in any way he could the observations in the use of the serum.

REVIEWS AND NOTICES OF BOOKS

Cardiovascular Function

Clinical Investigation of Cardiovascular Function. By V. PACHON, Associate Member of the Academy of Medicine, Professor of Physiology in the Faculty of Medicine; and R. FABRE, Professor of Physiology, Director and Examiner in the Faculty of Medicine of Bordeaux. London: Kegan Paul, Trench, Trübner and Co. 1934. Pp. 252. 15*s*.

THE Anglo-French Library of Medical and Biological Science has as its object the publication in English and French of monographs on their special subjects written by authors of distinction. This is a good example of its productions. Prof. Pachon is already well known in England through his publications on oscillometry, and it is appropriate that his new book on the clinical investigation of cardiovascular function should be translated by Dr. Halls Dally who was one of the first to introduce Prof. Pachon's oscillometer to British clinicians. The chief thesis here expounded is that to test a patient adequately for functional efficiency it is necessary to examine him in a dynamic state and as far as possible after activity comparable with that of his normal life; in other words it is the physiology and not the anatomy of the patient that is important. The second point made is that not only total but partial inefficiency should be studied and that consideration should be given to the different elements which "collectively and by their functional harmony constitute a perfect physiological equilibrium." An account is given of the procedures used in estimating cardiovascular function, only such methods being described as have been selected by the authors for their own use.

The first part of the book is concerned with cardiac investigation and includes a detailed description of cardiography in the left lateral recumbent posture which the authors claim to be a specific method of functional investigation of the heart beat introduced into clinical medicine by Pachon himself in 1902. This is followed by a description of jugular phlebography and well-illustrated sections on electrocardiography and on radiography. The second part of the work is devoted to vascular investigation, the methods described including sphygmomanometry and oscillometry. Physiological variations of arterial pressure are discussed and also the functional investigation of the capillary and venous circulation. It is disappointing that a really satisfactory functional test for cardiac efficiency is still to seek.

This book, to quote the editorial note, contains "the fruits of a life-time of labour" and will well repay careful study.

The Patient and the Weather

By WILLIAM F. PETERSEN, M.D., assisted by MARGARET E. MILLIKEN, S.M. Vol. II., *Autonomic Disintegration.* Michigan: Edwards Bros., Inc. 1934. Pp. 530. $6.50.

THIS is the second volume of a series to appear, the third volume of which has already been reviewed in our columns (see THE LANCET, 1934, ii., 991). The first and subsequent volumes—for there are three or four more to come—are in preparation and we understand are held back pending the securing of further meteorological data. This volume is made up of observations on the individual who is unusually responsive to environment, that is to say, in whom clinical reflections become apparent because the influence of climate is particularly able to be recognised for its amplitude. Acknowledgment of coöperation is made to the many colleagues who have supplied instances which fall under intestinal, ophthalmological, dental, and dermatological headings, and there are particularly interesting sections in the chapter which deals with asthma and arthritis. The literature referred to in this chapter is arranged as an alphabetical list which fills some four columns of close printing; the references are placed under the sections dealing with the various manifestations, and the authorities cited seem to be very seldom British.

The authors hold that investigation of disease in connexion with climate has now passed from observation in which the effect of meteorological environment is apparent only from functional manifestations to the special field where actual tissue necrosis may be involved. The subject of arthritis, for instance, is discussed with relation to the many factors that may be involved under the manifold conditions which are implied under that title. There are detailed studies of many individual cases and the whole of this section is profusely supplemented by graphs in illustration of clinical episodes and their relation to temperature, climate, and physical geography. A similar pattern dictates the arrangement of other sections, and no review in detail of a volume of such huge size, and so packed with references and cross references to other literature, would assist any reader in a practical manner. But general commendation of a great effort, in many ways satisfactorily accomplished, may be expressed. The individual case records used in the work are those of the Psychiatric Institute of the University of Illinois and in most instances will be found comprehensive.

Cataract

Its Etiology and Treatment. By CLYDE A. CLAPP, M.D., F.A.C.S., Associate Professor of Ophthalmology, Johns Hopkins University. London: Henry Kimpton. 1934. Pp. 254. 18*s*.

THE lens and its anomalies, including cataract, are here considered apart from other diseases of the eye. The book begins with two chapters by Miss Ida Mann on the development and comparative anatomy of the lens. The chapter on structure includes the new knowledge that we owe to the slit lamp. The chief function of the lens is to focus rays of light on to the retina but it also acts as a filter whereby certain harmful rays such as the ultra-violet are to a large extent removed. In connexion with focusing, the theory of accommodation is discussed, but the author hardly gets us beyond the usual statement of the rival theories of Helmholtz and Tscherning. The key to a more satisfactory explanation is probably to be found in the respective functions of the three parts of the ciliary muscle, but this aspect of the subject is left vague. After chapters on the chemical composition and growth in size of the lens through life, the various forms of cataract are described—congenital, traumatic, secondary, and senile. Perhaps disproportionate attention is paid to the so-called non-operative treatment of cataract and to the operation of couching as practised in India. About one-third of the book is devoted to the different methods of cataract extraction and their modifications. The "combined extraction" has now become the safest operation and is favoured by most operators, though the details

of procedure vary. The variations concern the method of making the incision and the conjunctival flap; the method of opening the capsule; the use of preliminary iridectomy; the irrigation of the anterior chamber to get rid of soft lens substance; and the employment of conjunctival sutures. The removal of the lens in its capsule by the "Indian Smith operation" is also briefly described—with its modifications by Knapp, favoured in America, and by A. H. Sinclair of Edinburgh—and also the suction operation of Barraquer. None of them, however, is generally performed by English or American surgeons, whose choice lies rather between the "combined" operation and the "simple" one without iridectomy.

This book gives the generally accepted facts about cataract in an easily readable form. It is well illustrated, well indexed, and well printed.

The Biochemistry of Medicine

Second edition. By A. T. CAMERON, M.A., D.Sc., F.I.C., F.R.S.C., Professor of Biochemistry, Faculty of Medicine, University of Manitoba; Biochemist, Winnipeg General Hospital; and C. R. GILMOUR, M.D., C.M., F.R.C.P. (C.), Professor of Medicine and Clinical Medicine, University of Manitoba; Physician, Winnipeg General Hospital. London: J. and A. Churchill Ltd. 1935. Pp. 518. 21*s*.

Prof. Cameron is well known as a writer of accurate and well-informed works on biochemistry. His association with a clinician, Dr. C. R. Gilmour, has resulted in the addition of a very useful book to the literature of biochemistry as applied to medicine. Much information is here crammed deftly into small space. Our only suggestion concerns the inclusion of detailed descriptions of pieces of work of doubtful value, and in some cases of work which has definitely been disproved, in which obviously the authors themselves have no faith. A good example of this can be seen in the section on the biochemistry of tumours, where several paragraphs are devoted to an entirely discredited serum reaction. This space could have been employed much better by giving a succinct account of, let us say, Warburg's work on the metabolism of malignant and normal tissues, or by a biochemical consideration of the more recent work of Peyton Rous, R. E. Shope, and other investigators. The summary of recent advances in the endocrine glands is a very good one; we would have liked to have seen further details concerning the inter-relationship of the sterol group, the vitamins, and the sex hormones.

The work as a whole is excellent.

A Text-book of Pathology

An Introduction to Medicine. Second edition. By WILLIAM BOYD, M.D., M.R.C.P. Edin., F.R.C.P. Lond., Dipl. Psych., F.R.S.C., Professor of Pathology in the University of Manitoba; Pathologist to the Winnipeg General Hospital. London: Henry Kimpton. 1934. Pp. 1047. 45*s*.

Prof. Boyd's books are notable for their clear exposition and easy style, and through them he has made himself widely known as a teacher of pathology. This second edition of his Text-book of Pathology shows considerable alterations, especially in the arrangement of the section on general pathology. Degenerations are dealt with first, then circulatory disturbances, leading up to inflammation and repair, immunity, bacterial infections, and animal parasites. The chapter on bacterial infections has been rearranged. The section on general pathology concludes with a valuable innovation—a chapter on heredity in disease in which Prof. Boyd discusses in a very brief but illuminating way the theory of inheritance.

The work is still very readable. It covers the subject thoroughly, and the material presented is well chosen and set out rather dogmatically, so that it gives the student clear and unconfused impressions of pathological processes without burdening him with controversial issues. The illustrations are plentiful and well chosen, and the whole work is handsomely produced.

Essays on Chronic and Familial Syphilis

By GRIFFITH EVANS, M.A., D.M., F.R.C.S., Hon. Surgeon, Caernarvonshire and Anglesey Infirmary. Bristol: John Wright and Sons Ltd. 1934. Pp. 91. 7*s*. 6*d*.

THIS small book consists of a series of essays upon an aspect of syphilis which has received little attention—except in France. The author bases his observations upon certain propositions which though not definitely proven are accepted by most syphilologists: (1) that the spirochæte of syphilis has a "dormant, granular" phase, in addition to the spiral form; (2) that untreated syphilis may be transmitted to the third generation; and (3) that even in the absence of a positive Wassermann reaction a diagnosis of syphilis can sometimes be made. He gives a list of the leading symptoms which he has noted in 100 consecutive cases of what he regards as chronic or familial syphilis—the two commonest being abdominal pain and chronic headache which were present together in 41 of the cases. Amongst the physical signs in these same 100 cases, "unequal reacting pupils" were noted in no less than 50, and in the author's experience the most suggestive common signs of latent syphilis are, in addition to inequality of the pupils, smooth, fissured, or fibrotic tongue, persistent tachycardia, and chronic low pyrexia. The presence of these symptoms should, in Mr. Evans's view, lead to the suspicion of syphilis. Acting on these assumptions the author has treated his patients on antisyphilitic lines, generally with marked benefit.

These essays, which were awarded the gold medal of the Hunterian Society, deal with syphilis in relation to nervous dyspepsia, the chronic abdomen, nervous dysphagia, glossitis, and cancer. They provide a thoughtful contribution to our knowledge of syphilis in its less recognised form.

British Journal of Surgery

THE April issue (Vol. XXII., No. 8) includes the following papers:—Progressive Post-operative Gangrene of the Skin, by A. M. Stewart-Wallace (London). The third case to be recorded in England. The gangrene followed drainage of an empyema, and was very extensive, causing death after 32 weeks. The 37 reported cases are reviewed, and treatment by complete excision is recommended.—Adenoma of the Duodenum, by B. R. Sworn and J. Menton (Stafford). The tumour was discovered and removed during an operation of partial gastrectomy for gastric ulcer. It did not apparently add to the symptoms of the case. It proved to be polypoid, and consisted of a hyperplasia of the duodenal glands in a loose stroma.—Measured Dosage in the

Radium Treatment of Carcinoma of the Urinary Bladder, by R. G. Hutchison (Manchester). Open exposure and the use of radon seeds are advocated. A circular distribution of the seed is described, and the calculations required to ensure as uniform as possible a dosage over the field have been reduced to convenient clinical tables.—Interinnomino-abdominal (Hind-quarter) Amputation, by G. Gordon-Taylor and Philip Wiles (London). An account of 5 cases, of which 3 were successful. Particular attention is drawn to the importance of blood transfusion and care in turning the patient during the operation.—The Pathology of Congenital Genu Recurvatum, by D. Stewart Middleton (Edinburgh). A case is described which was successfully treated at the age of 18 months by division of the quadriceps tendon and of its lateral expansions. The condition is considered to be an intrauterine degeneration of muscle-fibres in the quadriceps femoris.—Observations on Fistula-in-Ano in Relation to Perianal Intramuscular Glands, with reports on 3 cases, by Sir Charles Gordon-Watson and Harold Dodd (London). Histological evidence is submitted that infective processes in the perianal glands may be the starting-point of fistulæ and of ischiorectal abscesses.—Schimmelbusch's Disease of the Breast and Dr. A. Lacassagne's Experiments on Mice, by Sir Lenthal Cheatle (London). Lacassagne's observations on young male mice show that injections of œstrin are followed by a series of changes exhibiting a striking similarity in nature and sequence to those described by Cheatle as typical of Schimmelbusch's Disease. In the mouse the changes lead up to adeno-carcinoma.—Osteo-arthritis of the Hip-joint, by T. P. McMurray (Liverpool). The indications for the various forms of treatment are discussed. Manipulation in the early stages, and the Lorenz method of osteotomy are considered to be of most value.—The Pathogenesis of Paget's Disease of the Nipple and Associated Lesions, by Sir Robert Muir (Glasgow). Observations confirming that an intraduct carcinoma of the breast is the underlying cause of Paget's disease. The frequency of adeno-carcinoma is emphasised, as well as its association with ordinary breast carcinoma.—Paraplegia in Pott's Disease, with Special Reference to the Pathology and Ætiology, by R. Weeden Butler (Cambridge).—Pott's Paraplegia: Prognosis and Treatment, by H. J. Seddon (London). These two papers are complementary. In all 186 cases are reviewed; numerous pathological specimens have also been considered. The clinical course of paraplegia occurring at various stages, early and late, in the disease is correlated with the pathological lesions. The value of hyperextension in the prevention and cure of paraplegia, and of the operation of costotransversectomy, are especially stressed.—Skeletal Lipoid Granulomatosis, by John Fraser (Edinburgh). The disease is regarded as a reaction on the part of the reticulo-endothelial tissues to an excess of lipoid in the circulating fluids. Granulomatous tissue is produced in various situations, displacing, compressing, and causing atrophy. Exophthalmos, diabetes insipidus, and calvarial osseous defects are among the clinical results. Treatment is by deep radiotherapy, and cholesterol-free diet.—An Unusual Case of Bone Regeneration after Complete Diaphysectomy on Two Occasions, by J. W. S. Blacklock and W. Rankin. The case was one of acute osteomyelitis of the tibia. The regenerated bone had grown with the general growth of the child, and showed remarkably normal anatomical features.—The Treatment of Spasmodic Dysphagia by Sympathetic Denervation, by Lambert Rogers (London). Operations consisting of complete removal of both superior cervical sympathetic ganglia were carried out in November and December, 1934, and have given complete relief of symptoms.—On Osteo-arthritis in the Dorsal Intervertebral Joints. A study in Morbid Anatomy, by L. R. Shore (Cambridge). Includes an examination of the incidence at various vertebral levels and an interpretation of the findings in relation to mechanical stress.—Polyspondylitis Marginals Osteophytica, by L. R. Shore (Cambridge). The term is used to describe the common type of vertebral disease with "lipping" of the bodies. The underlying cause is considered to be loss of normal turgescence of the discs, and strain, ending in ossification, of the deep intervertebral ligaments.—Sympathectomy in the Treatment of Achalasia of the Cardia, by G. C. Knight (Research Laboratories of Royal College of Surgeons of England). The ætiology of achalasia and cardiospasm are considered, the various types of treatment are reviewed, and the rationale of sympathectomy is explained. An account of 3 cases thus treated is given.

Liverpool Medico-Chirurgical Journal

Hugh Owen Thomas's position among modern leaders of British surgery was well brought out in Mr. Frederick Watson's centenary volume dealing with his life and surgical principles and performances. The current number of the Liverpool Medico-Chirurgical Journal keeps alive our interest in Thomas, being dedicated to a centenary notice of the man who directly, and indirectly through his great pupil and nephew Robert Jones, dictated much of the theory and technique of modern bone surgery. Mr. T. P. McMurray, director of orthopædics in the University of Liverpool gives us in the Journal a detailed biography of Thomas made specially acceptable by the appropriate illustrations. His biography concludes by repeating one of Thomas's own frequent sayings—"I hope I shall not be remembered only as an inventor of splints, for any mechanical fool can do that; the idea to which they give effect is the important point." Such a narrow impression of Thomas's work will be removed by the action of the Liverpool Medical Institution, where it is intended to form a Hugh Owen Thomas and Robert Jones library of orthopædic surgery in which it is hoped that every phase of that branch of surgery will be represented. This excellent number of the Journal concludes with an essay on malignant tumours by Mr. Harry Platt, orthopædic surgeon to the Manchester Royal Infirmary, based upon an address delivered recently at the University of Liverpool, and noticed editorially in THE LANCET last week.

Italian Journal of Allergy

THE first number of *I Quaderni dell' Allergia*, an Italian bi-monthly publication devoted to the subject of allergy, contains a paper by J. Van Niekirk on the altered power of serum from allergic patients to combine with certain pigments. The author finds the blood-serum from cases of asthma, urticaria, and Quincke's œdema often, but not always, to have a reduced power of combining with pigment as compared with normal sera. This change, however, is not characteristic of the allergic state nor was it possible to establish a parallel between the clinical condition of the patient and the serum reactions. The other papers in this number deal with diagnostic intradermal reactions and climatic allergy. The highly specialised scope of the journal will appeal to research workers in this field. The annual subscription in this country is 80 lire.

CENTENARY OF THE BENGAL MEDICAL COLLEGE

(FROM A CORRESPONDENT)

THE Medical College of Calcutta is this year celebrating its centenary. The record of the first medical school in British India is interestingly told in the Centenary Volume. Before the days of the Medical College the surgeons recruited by the East India Company trained their own Indian assistants. These began as compounders and dressers and had to pass examinations before they were entitled to

higher rank and pay. The demand for these men increased, and there was need for a central institution where a more uniform and better system of education could be imparted. The first medical school was sanctioned in 1822 and was opened in October, 1824; it provided for the education of 20 students; instruction was in Sanscrit and Urdu; and the curriculum occupied three years. No dissections were attempted except of lower animals; but the students saw the post-mortems on persons dying in the General Hospital. Pharmacy seems to have been taught with particular care, for Dr. Bretton, the superintendent, in a report to the Medical Board detailed the tuition in the preparation of sulphate of soda, magnesia, muriatic and nitric acids, calomel, hyd. precip. rubrum, and spirits of wine from rice and goor (raw sugar); methods for the purification of benzoin, camphor, and sulphur were also taught. Dr. Bretton reported that the seniors are each made to describe the component parts of the brain, viscera, bowels, and the structure of the eye, and to answer questions. "The zeal and diligence with which the pupils prosecute their studies even in the least attainable part, i.e., anatomy, afford a very cheering prospect of their ultimately becoming one of the most useful class of servants in the service of the British Government in India." This prophecy has been amply fulfilled.

The Calcutta Native Medical Institution, as this school was called, continued till 1835. It had in succession as superintendent Dr. James Jamieson, remembered for his studies of cholera; Dr. Peter Bretton, a versatile author and an early member of a distinguished line of Calcutta ophthalmic surgeons; and Dr. John Tytler, an able Oriental scholar who translated many tracts for the benefit of the students. Tytler sturdily maintained that Indian pupils should be taught in their own vernaculars; but on this point there was much controversy, and the Rev. Dr. Duff, the founder of Scottish Churches College, Calcutta, seems to have advocated English as the medium. The Native Medical Institution had, however, defects, and in January, 1835, on the recommendation of a committee of inquiry, Lord William Bentinck, the Governor General, issued an order in Council decreeing that a new college should be opened to all classes of Indian youths without distinction of creed or caste, and that the instruction should be in English and in strict accordance with "the mode adopted in Europe."

The new Medical College opened in February, 1835, in the premises of the Old Petty Court Jail. The superintendent, Dr. M. J. Bramley, had one assistant, Dr. H. H. Goodeve; 50 students were admitted and the course of study was fixed at four years. The strong prejudice against anatomical dissections had to be overcome. Before the first year was completed Dr. Goodeve had a human body on the lecture table, and in January, 1836, his assistant, Pundit Madhu Sudan Gupta, with four courageous pupils, secretly accompanied Dr. Goodeve to an outhouse of the building, and Gupta began to dissect a body procured for a lecture. A portrait of Madhu Sudan Gupta was presented to the College in 1850 in commemoration of this achievement. It hangs in the anatomical lecture theatre of the present College, and is reproduced in the Centenary Volume. In less than two years practical anatomy had secured its place in the curriculum, and in 1848 Goodeve had a class of 250 "of all nations, colours, religions, and castes co-mingling together as freely and amicably as the more homogeneous frequenters of an European school."

Death exacted a heavy toll in these days; in 1837 Bramley, the first principal, died of fever at the age of 34. He was succeeded by Mr. David Hare, a well-known philanthropist, who was designated secretary of the council and treasurer. The professional staff was increased to five. It included as professor of chemistry Dr. W. B. O'Shaughnessy, who was later knighted, elected F.R.S., and became director-general of posts and telegraphs; as professor of botany, Dr. N. Wallich, M.D., F.R.S.; as professor of surgery, Dr. C. C. Egerton, an original Fellow of the Royal College of Surgeons. The surgeon superintendent of the Calcutta Native Hospital at the time was Dr. J. R. Martin, an original Fellow of the Royal College of Surgeons, later to be knighted, elected F.R.S., and to become the first President of the Medical Board of the India Office. In 1838 a ward of 20 beds was opened, the nucleus of the great hospital which now serves the Medical College. This was not the first hospital in Calcutta, for, as long ago as 1707, the Council of Fort William built a hospital on a "convenient spot close to the Burial Ground." It was north of where St. John's Church now stands and near the mausoleum of Job Charnock. The first Indian hospital was opened in 1793 in Chitpur Road, and three years later was moved to "the open and airy road of Dhurrumtollah" where there were then only three or four houses. It was moved later to Strand Road and is now the Mayo Hospital.

In 1845 the curriculum was remodelled and extended to five years. The following year the Bengal Medical College was the first educational institution in British India to be recognised by the University of London, the Royal College of Surgeons, England, and the Society of Apothecaries, and Dr. Goodeve brought four students to England, all of whom passed the final M.B. London, two proceeding to the M.D. Meanwhile a shorter curriculum with teaching in the vernacular was established to meet the demand for subordinate medical officers in army and civil hospitals. The year 1848 saw the laying of the foundation-stone of the medical college hospital, and four years later it was opened. The Calcutta University was founded in 1857, and with it the Medical College was affiliated. Students henceforth were required to obtain a licence in medicine and surgery or the degree of M.B. or M.D. The first woman student was admitted in 1884, and the first women graduates obtained their degrees in 1889. Nurses seem to have been introduced in 1859; and from 1881 till 1910 the training of the nurses was undertaken by the Clewer sisters from England.

From these early days the history of the Medical College and its hospital has been one of development and expansion. The students now number 754. The College and the associated hospitals cover an area of over 55 acres and adjoining are the daughter institutions, the School of Tropical Medicine and the All-India Institute of Hygiene, the one due to the initiative and enthusiasm of Sir Leonard Rogers and the other to that of Sir John Megaw and the generosity of the Rockefeller Foundation. The College and the group of institutions with which it is surrounded is a worthy memorial to the succession of teachers and administrators supplied by the Indian Medical Service. The end of the first century of its existence coincides with the handing over of the College to the care of those, many of whom are its own sons, and the change is even shown in the new college crest. Their names, it will be hoped, will add to the high reputation won for the College by such predecessors as Jamieson, Martin, Goodeve, O'Shaughnessy, Murchison, Fayrer, Macnamara, D. Cunningham, Lyon, Waddell, Prain, Rogers, and their colleagues.

THE LANCET

LONDON: SATURDAY, MAY 11, 1935

THE POST-GRADUATE SCHOOL

THE opening by the KING on Monday next of the British Postgraduate Medical School at Hammersmith is the biggest event in the history of medical education which most of us will witness. Some may just remember the founding of an undergraduate medical school but nowhere in the Empire is to be found a centre of post-graduate medical education at all comparable with those which are available to the student on the continent and in America. For the newly qualified student, for the general practitioner, for all medical officers employed by the State, the new school will make provision to meet their own particular requirements. In addition the school hopes to be able to provide for more than purely local requirements. Every year many doctors visit London from overseas. There are officers of the naval, military, Indian, and colonial services on leave or study leave, medical missionaries from the outskirts of the Empire, teachers in foreign medical schools, and consultants from our Dominions. Many of these have been coping single-handed with difficult medical problems and large masses of population for whom they are the sole representatives of Western medicine. They have neither had time nor opportunity to discuss their problems with other colleagues. Their knowledge of recent advances is derived solely from the articles they read in the medical journals. They require guidance and advice to make the best use of the experience available. From the more advanced Dominions many students visit London in the hope of doing post-graduate work. They have been educated to regard London as a great centre of medical knowledge and research. Up to the present they have found difficulty in obtaining facilities to follow up their own particular lines of work. Often they have returned discouraged and disheartened or have gone on to continental clinics. For all these overseas visitors the school hopes to provide opportunities for work and means to further their education. The benefit of such work will be felt far beyond the limits of the United Kingdom. Many visitors from overseas complain that much of the instruction available until now has been didactic and impersonal. The school hopes to remedy this and to conduct its teaching not so much by set courses, as by bringing the student and his teachers into personal contact over their cases in the wards. The intimate association thus established will have its effect long after they have left the school.

This is the practical side of the school. There is another side and one which is equally important. It is not merely a gesture that the school forms part of the University of London. It is the intention that the scientific side of medicine should develop pari passu with the practical side. Speak as we may of the science and art of medicine it is only recently that the science of medicine has been recognised as something more than the investigation, by scientific methods, of problems having immediate practical application. One of the main objects of this school will be to study problems in the scientific spirit—to carry on investigation, not because of the immediate practical value of the solution of the problem, but for the advancement of knowledge. With this object in view facilities for research are being provided. Not only are laboratories necessary, and funds to equip them, but fellowships and staffs sufficiently large to relieve the senior members of much of their routine teaching. Encouragement will be given to young graduates desirous of following up lines of research or anxious to take up the academic side of medicine and they will be provided with facilities to work and study in the school. To men having the necessary qualifications and inclination to pursue research, rather than the more profitable branches of practice, the schools will provide the opportunities. Its object will be no less than to provide a training ground for the future teachers of scientific medicine.

The establishment of this school has aroused world-wide interest. Inquiries have been received from all over the world. Visitors have come from Tashkent and Teheran; students are already attending from New Zealand, India, Persia, Spain, and Switzerland. The ambition of all those concerned in its founding and working is that the school shall become a centre of medical education and research of international repute, worthy of the British Empire and commensurate with its size, responsibility, and influence.

THE SURGERY OF CARBUNCLE

DURING the last decade or two a subtle but notable change has come over the general surgical outlook. The anatomical, mechanistic views which so long held sway have gradually given place to a much broader and more rational conception of surgery. The modern surgeon recognises that vital processes are at work and that his gross interventions do no more than direct or divert natural processes into channels that lead to the ascendancy of reparative activity. With this altered mental conception of surgery many changes have taken place, mostly in the direction of restricting operative measures. Surgery is shrinking in its scope. No longer does the diagnosis of tuberculous disease of the lymphatic glands or joints imply operative excision, or the discovery of a movable kidney bring with it an inevitable fixation, or that of severe constipation a short-circuit. In no department of surgery has the modern critical spirit been more pronounced than in the treatment of septic infections. We have seen the delayed treatment of appendicitis, the

delayed opening of empyema, the limited operations for osteomyelitis and cellulitis, the non-operative management of carbuncle, and the closed treatment of septic compound fractures. In a paper published in THE LANCET on April 13th, Dr. J. T. INGRAM, dealing with certain septic infections of the skin, goes even further. Writing of whitlows he declares dry heat to be always better than wet, macerating heat; he holds that septic perionychia should never be treated surgically, and he makes an earnest plea for the conservative treatment of boils and carbuncles, believing firmly that these lesions should never be subjected to operative trauma. Similarly Mr. P. H. MITCHINER, from the study of statistics of cases treated at St. Thomas's Hospital, has come to the conclusion, in common with other English and continental surgeons, that operating upon a facial carbuncle raises the mortality-rate.[1]

It is a maxim of surgical therapy, dating from antiquity and based upon countless observations of generations of men, that evacuation of pus is a definitely curative act. Thousands of experiments have proved beyond any doubt the essential truth of this tenet. Hence the assertion that a boil of any size should be treated by an occlusive dressing is not likely to be accepted by surgeons unless it is backed by overwhelming evidence. At the same time the critical attention given to the subject is useful if it does no more than emphasise the undesirability of early surgical intervention in most septic infections. One of the beneficent results of the closer study of these diseases and the reconsideration of surgical practice has been the greater recognition of the predominating rôle of the tissues. Whether it be a boil, a carbuncle, or an acute osteomyelitis, limitation of the disease must finally be brought about by a combination of general and local body reactions. Which of these is the more important it is impossible with our present knowledge to say, but it is an interesting and significant observation that cellulitis may clear up in one region of the body while it may be progressing in another even to a fatal termination. What the insistence on abstention from surgical incision does emphasise is that nothing must be done which might in any way disturb the natural indispensable local reactions of the tissue cells. It is a perfect truth to say that, under certain circumstances, the incision of a boil, a carbuncle, a cellulitis, or a whitlow, is a meddlesome, unnecessary, harmful, and even death-dealing action, but it would be robbing surgery of one of its most powerful therapeutic weapons to forbid such incisions under all conditions. Indeed most surgeons would claim that their personal experience shows that after a certain local response of tissue cells has occurred around a carbuncle a judicious incision not only gives great subjective relief but does seem to hasten the healing process. Scraping, because of the traumatisation involved, always appears to be harmful, but it is difficult not to believe that the simple incision which relieves tension and lessens pain does not also have a directly curative effect by allowing fresh immune plasma access to the formerly tightly distended tissue spaces. It is the selection of the correct time for such incisions that is of such great importance and in this lies the art of surgery, for as yet we have no rules, no measurable phenomena or reactions which can tell us just when the necessary tissue response has taken place.

The decision needs particular care and thought when it is a question of operating on facial boils and carbuncles, especially those of the upper lip and beside the nose; for in such cases dissemination by the veins to the cavernous sinus is not uncommon. Anatomical arrangements no doubt play the major part in this terrible result. Unlike other regions of the body, the face has no deep fascia to limit the infection to the subcutaneous tissue, and the infective process accordingly has direct access to muscles, with their abundant venous channels, and to the nearby facial trunk. Its spread is probably helped also by the involuntary movement of the muscles of facial expression which cannot be wholly checked. In Mr. MITCHINER'S figures from St. Thomas's Hospital 2 out of 10 patients with facial carbuncle in whom an incision was made died, whilst of 73 treated conservatively only 5 succumbed. It is true that this series of cases is not large but there are other series from different clinics which point the same way, and though the evidence for the policy of conservatism for facial carbuncle can certainly not be regarded as conclusive, it clearly needs careful consideration. Of other methods of treating carbuncles excision must receive attention in view of the experience at St. Thomas's Hospital. If excision is done, it must be wide to be effective and the better results of excision (over incision) may have been due to the fact that only the smaller lesions were excised. Certainly most surgeons who have practised both measures would agree that healing is much delayed after excision. Whether a carbuncle is treated conservatively or by incision, it is remarkable how much of the epithelium seems to escape destruction by the septic process and survives to form points of regeneration; but all this advantage is lost when it is excised. Incision by the diathermy knife also has its advocates, though it is difficult to see how this can be an improvement on knife incision and indeed how it can give any relief at all. The object of an incision is to provide an exit for pathological humours and to give free flow to immune plasma—both of which objects are frustrated by the diathermy knife, which seals as it cuts. Indeed it is curious how very little is really known of the effect of different methods of treatment on so common a malady. The collection of a mass of controlled data and their correlation are urgently required, and it is essential that we should know how the results of the most satisfactory operative technique compare with those of the short-wave and X ray therapy now widely recommended. Surgical research could hardly be devoted to more useful ends.

[1] THE LANCET, March 2nd, 1935, p. 507.

A DECADE OF PROGRESS IN ANÆSTHETICS

IN a retrospect addressed to the section of anæsthetics of the Royal Society of Medicine on Friday last Dr. C. F. HADFIELD spoke of the work, covering the last decade, of the Anæsthetics Committee jointly set up in 1924 by the Medical Research Council and the section. He recalled its original personnel; this was composed of three anæsthetists, J. BLOMFIELD, C. F. HADFIELD, and FRANCIS SHIPWAY, with three other men of science, F. G. DONNAN, F.R.S., H. H. DALE, F.R.S., and M. S. PEMBREY, F.R.S. Prof. PEMBREY died in 1934, but the others are still serving and to their number have been added Prof. C. A. PANNETT and Dr. W. R. SPURRELL, reader in physiology at Guy's Hospital.

The first important work undertaken by the committee was directed towards the investigation of well-known agents and concerned nitrous oxide gas. Complaints were being made of undesirable symptoms following the inhalation of laughing gas, which had become popular as an anæsthetic during the war, while at that time nitrous oxide was being freely tried by men little versed in its use, at any rate for major surgery. It was suggested in certain quarters that the gas was to blame, and that probably an impure or faulty agent was being provided by the manufacturers. A thorough investigation by the committee of the evidence brought forward, together with scientific as well as clinical testing of the suspected samples, resulted in a complete vindication of the products on the market. The lesson was enforced that when undesirable symptoms arise during anæsthesia it is rarely the drug that should be blamed; most often the fault lies with the administration of it. A further advantage has been gained from the work on nitrous oxide; this compound had not hitherto been included in the British Pharmacopœia, where it now appears complete with tests and standard of purity. That well-known brands of ether and chloroform are as reliable and free from any but negligible amounts of impurity as is nitrous oxide was also proved by the investigations of the committee. Ether, especially, has received a considerable amount of attention since, a few years ago, a suggestion was made by one or two chemists and anæsthetists of standing that pure ether is not itself an effective anæsthetic and that the properties for which it is valued and used are really the properties of its impurities. The committee was able to organise experimental and clinical tests which disproved this theory and established clearly the anæsthetic properties as those of ether itself. Dr. HADFIELD showed also how valuable have been the efforts of the committee in obtaining duty-free ethyl alcohol for the manufacture of pure ether, and in establishing a standard preparation in the British Pharmacopœia. The official standard now laid down is very stringent. To make ether of the new B.P. standard from methylated spirit is nearly impossible. The statement that pure ether can be improved by various alterations and additions occurs from time to time; but the B.P. standard for anæsthetic ether is now so strict that it is impossible to believe that any two ethers conforming to it can differ from one another in potency, odour, irritating qualities, or any other significant feature. Any ether good enough to pass the B.P. tests, and to retain the purity thus assured, may be regarded as completely satisfactory for all anæsthetic purposes. Dr. HADFIELD went on to describe the interesting experiments carried out for the committee by the late Prof. H. B. DIXON, F.R.S., on the ignition points of various gases. These led among other lessons to the important practical one that nitrous oxide is not the inert gas that many anæsthetists have supposed it to be, but may be a formidable agent in promoting explosion in certain conditions of temperature and in the association with other gases.

Perhaps even more valuable than its researches into the use of familiar agents has been the work of the committee in connexion with newly introduced anæsthetics. The procedure adopted of enlisting the coöperation of chemical firms has worked admirably in the public interest. It has been made possible for these firms to introduce a new anæsthetic to the profession with the hall-mark conferred on it by a favourable report from a research body, which had the opportunity to submit the new product to the clinical and laboratory tests thought desirable. The first anæsthetic dealt with in this manner was Avertin. This had been made, and was already being freely used, in Germany, before the distributors in this country received supplies. Instead of seeking at once to bring these to the notice of the medical profession the manufacturers agreed not to release avertin except to individuals named by the committee. Only when tests had been completed, and a report on their results had appeared in the medical journals, did the manufacturers offer the drug for free sale. This is clearly an excellent way of introducing into practice potent drugs, such as anæsthetics, whose value and safety depend largely on the conditions of their employment. The practitioner may well be misled by glowing accounts arising from the enthusiasm of a pioneer who has blazed a fresh trail in anæsthesia. He may read: "here is an agent which produces perfect muscular relaxation, is pleasant to take, has no undesirable after-effects, and is quite safe." These words represent the terms under which have been introduced many anæsthetics which time and experience have almost completely removed from practice; but many a tragedy may have happened in the interim.

There are anæsthetic drugs whose methods of employment are suitable only for the use of those who are constantly giving anæsthetics; and there are those which the occasional anæsthetist can employ with safety; it is especially in the differentiation between them that the committee can give help. How to discern which agent or method belongs to the former and which to the latter group is by no means easy for the non-specialist, and his difficulties are increased by the speed with which his patients

gain, from the daily press, a superficial acquaintance with the properties of the latest innovations in anæsthetics. When the patient demands the wonderful drug which "simply sends you straight off—like that!" the doctor must ascertain first and foremost whether he dare try it himself or whether it is a drug that should only be given by an expert, quite apart from its suitability in any particular case. Most of the effective basal anæsthetics, for example, can hardly be used to the best advantage except by those who are constantly engaged with anæsthetics; yet almost the latest barbiturate, Evipan, has such value for the general practitioner that it would be well worth his while to master the technique of its administration, and make himself familiar with its risks, indications, and contra-indications for its use. Cyclopropane, on the other hand, has been shown by the work of the committee to be a potent anæsthetic with many valuable qualities, but essentially one which should be used only by experienced anæsthetists. Acetylene, Butylene, Cyclohexine, Dimethyl ether, Ethylene, Propylene, and Vinethene are among the many other agents which have been investigated by the committee, whose activities have contributed directly or indirectly to the inclusion of several gases in the latest edition of the British Pharmacopœia, notably nitrous oxide, carbon dioxide, ethylene, and oxygen. The work done by the committee, in fact, gives a good illustration of the immense value of close coöperation between those engaged in a solely practical and clinical branch of medicine and the purely scientific worker.

ANTISTREPTOCOCCAL SERA IN PUERPERAL FEVER

THAT these sera possess protective value, often of a very high order, can be readily demonstrated, but quite commonly, a serum found to be potent when used prophylactically, will prove of little value in experiments designed to test its curative properties. Bearing this in mind it will be realised that at times in the serum therapy of human disease, we expect from these sera something which is beyond their power to achieve. Our astonishment should be not that they sometimes fail us, but that they so often seem to have therapeutic value. Prior to the demonstration that the hæmolytic streptococcus produced a soluble toxin, antisera prepared against these micro-organisms were of the antibacterial type, and it has to be admitted that the sera used in the treatment of streptococcal infections in man has been, at the best, disappointing. But with the production of potent antitoxic streptococcal sera, of which, of course, scarlatinal antitoxin is the outstanding example, and the demonstration that all toxigenic strains of *S. hæmolyticus* produced the same toxin, it was hoped that here, at last, was a type of serum which would be of real service in clinical medicine. Has this hope been realised? As far as the use of antitoxin in the treatment of scarlet fever is concerned the answer would appear to be in the affirmative. It has to be remembered, however, that in scarlet fever one is dealing with a type of hæmolytic streptococcus which, though highly toxigenic, is not very invasive, and it is precisely in these circumstances that one would expect such a serum to be effective. Can such a serum influence favourably the course of infection due to a hæmolytic streptococcus of invasive tendency? The answer to this question is by no means clear. Some observers speak enthusiastically of their experience with streptococcus antitoxin, others doubt its efficacy, some think even that the serum may at times be harmful.

In a paper appearing elsewhere in this issue Dr. LEONARD COLEBROOK discusses the use of antistreptococcal serum in the treatment of puerperal fever. He has collected 69 cases which had received serum prior to admission to Queen Charlotte's Hospital—antistreptococcal sera have not been used in the isolation block in this hospital—and has contrasted the results obtained in this group with cases not treated with serum. He admits that he has not been able to obtain complete details of the serum treatment in every case, but the information obtained from the medical men who treated these patients before sending them to Queen Charlotte's shows that only 30 out of the 69 were known to have received concentrated scarlatinal antitoxin; the others had "anti-streptococcal serum." The amount of serum administered varied from 10 to 140 c.cm., mostly given by the intramuscular route. There was no evidence that the cases receiving serum differed materially in other respects from the unselected admissions not treated with serum. The percentage case-mortality in these two groups is somewhat unexpected. In the first group—those receiving serum—there were 21 deaths giving a case-mortality of about 30 per cent., whereas in the group of 932 cases which received no serum 108 died, a case-mortality of about 11 per cent. It should be added that bacteriological examination revealed the hæmolytic streptococcus as the infecting agent in 40 and 346 of the two groups respectively; there were 29 patients in the serum-treated group in which no one could expect the serum to be beneficial. But if comparison is limited to those in the two groups known to be infected with the streptococcus, the case-mortality still works out unfavourably for serum, 45 and 22 per cent. respectively. In addition to these figures of his own, Dr. COLEBROOK cites the observations of BENSON and RANKIN on 114 cases of puerperal infection from whose blood hæmolytic streptococci were grown in every case. Half of this group was treated with serum (37 with scarlatinal antitoxin and 20 with puerperal anti-streptococcus serum); the other half served as controls. The mortality-rate was 75 per cent. in the serum-treated group and 72 per cent. in the controls. All will agree with Dr. COLEBROOK'S conclusion that such evidence does not support the use of antiserum in the treatment of hæmolytic streptococcal infections in man, at any rate in infections of the invasive type. He naturally hesitates to ascribe to the serum the higher mortality in his serum-treated group, but, as he

points out, there is experimental evidence that an inappropriate antistreptococcal serum or even normal horse-serum may have a deleterious action on the course of the disease. This would not apply, of course, to normal *human* serum which has been used by some clinicians to supply a deficiency of complement in the treatment of septicæmia.

Whether or not with increasing knowledge of the hæmolytic streptococci we shall be in a position to devise sera to combat those infections not primarily toxigenic only the future will disclose. The work of F. T. CADHAM, which was referred to at length in a recent issue of this journal, is an attempt to provide a solution to this problem. In the meantime however Dr. COLEBROOK'S plea for the abandonment of the indiscriminate use of streptococcal antisera in puerperal and surgical sepsis should receive serious attention. It is recognised, though not always remembered, that even under experimental conditions the various sera prepared against bacteria or their toxins often have but little curative action.

ANNOTATIONS

THE JUBILEE FESTIVAL

THE Jubilee ceremonial was a complete success; its object was attained. The King and Queen received an acclaim of personal loyalty and affection such as few, if any, reigning sovereigns have ever experienced; a precocious summer day lent a splendour to proceedings which, despite the gorgeousness of trappings and accessories, were of a simple nature; and organisation of a thorough kind averted the dangers inherent in the massing of crowds. The total size of the crowds which, from stands, balconies, and roofs, from trees, lamp-posts, and walls, from pavement, windowsill, and gutter, saw the Royal procession pass, may be capable of near estimation by experts on such matters; but whatever it was, it was tremendous. And the casualty roll, in proportion to the numbers involved, appears to have been negligible. The whole parade of the St John's Ambulance Brigade was in charge of Captain W. Goodley, M.C., the commissioner of the London Brigade. There were on duty 3000 men and 1000 women. Fifty-seven doctors were also posted along the line of route. There were 71 stations and 25 ambulances. Dr. Ernest McIntyre was in charge of the ambulance arrangements inside the cathedral. In all 7500 cases were treated along the route. In the evening members of the brigade, who had been on duty since 8 A.M., were stationed at the floodlighting and bonfires, and many of them remained on duty until 2 and 3 A.M. The total number of casualties treated during the evening has not yet been received. Members of the brigade will be on duty every evening this week from 8 P.M., and there will be 18 stations in the neighbourhood of the floodlighting. The speed and efficiency of the work rendered by the brigade during the procession were objects of general admiration and in particular impressed the numerous foreign visitors unofficially present.

ROYAL ACADEMY EXHIBITION

THE 167th Exhibition of the Royal Academy of Arts was opened on Friday last, and may be considered fairly to represent modern tendencies on the part of the majority of the public, which tendencies must be responded to by the majority of artists. What may seem very individual tastes are also met at this exhibition by very individual exponents. Among the oil paintings the resolution to be modern and to be different is certainly strained to the point of making some of the representations appear distorted to the amateur or unaccustomed eye, but a good proportion of them meet a desire for beauty, and that is what the majority of people hope to satisfy when looking at pictures. The circumstances of social life to-day have led the class that is best able to buy pictures to live in smaller rooms, and no doubt the exhibitions in the Academy galleries have been rendered more pleasing by the absence of the overcrowding formerly brought about through the size of many of the exhibits. Immense landscapes are few this year, and detailed stories in colour are fewer. With the disappearance of the anecdotal picture all scenes of medical life have gone from the walls, and our profession only enters the exhibition through the medium of the portraits of certain of its members. Among these may be noted a sympathetic and workmanlike portrait of Sir George Newman by Miss M. L. Williams; the presentation portrait of the veteran Sir James Crichton Browne by Mr. Oswald Birley; and an excellent portrait of Dr. G. F. Still by Mr. Gerald Kelly, R.A., which is destined to be hung in King's College Hospital, London. A picture from the brush of Mr. F. W. Elmlie, A.R.A., will take the eye as a skilful piece of work; this is a presentation portrait of Lieut.-Colonel Samman in character as Master of the Society of Apothecaries of London. The portrait of Prof. Cunningham M'Lennan, F.R.S., by Mr. Augustus John, R.A., may fairly be included in a medical category, as Prof. M'Lennan, a distinguished physicist and physiologist, shared the Nobel prize in medicine in 1923.

ARE ANTIBODIES PROTEINS?

THE nature of antibodies is not of theoretical interest only, for if they were shown not to be proteins there would be a hope of making active protein-free preparations from antisera, and thereby avoiding the risks of serum sickness and anaphylaxis. Almost all investigators who have attempted to prepare antibodies free from protein have reported failures, however, and in most of the few instances in which success has been recorded, the antibody solutions have been so weak that their protein content would be below the range of the not very delicate tests used. One of the claims to which this explanation did not apply was that of M. Frankel and L. Olitzki, but Rosenheim [1] has lately reported a complete failure to repeat their experiments. Moreover, the less direct methods of investigation all point to the protein nature of antibodies. For example, in reactions in which a precipitate is formed, the precipitate contains the antigen together with protein from the antiserum. It might be supposed that the protein thus precipitated from the antiserum was either the actual antibody or non-specific protein adsorbed on the antigen-antibody complex. Recent work has shown that the amount of protein precipitable from a given amount of an antiserum is constant. Heidelberger and Kendall [2] have confirmed

[1] Rosenheim, A. H.: Jour. Path. and Bact., 1935, xl., 75.
[2] Heidelberger, M., and Kendall, F. E.: Jour. Exp. Med., 1934, xliv., 529.

the original contention of Marrack and Smith [3] that the amount precipitated is independent of the concentration of non-specific protein in the reacting mixture. Heidelberger and Kendall in 1934, and Dean, Taylor, and Adair [4] this year found that the same amount of protein was precipitated from the antiserum, whether the precipitation took place in one stage or in two; while Heidelberger and Kabat [5] have shown that pneumococci when agglutinated carry down with them from a given amount of antiserum the same amount of protein as is precipitated by the corresponding polysaccharide. These experiments strongly support the theory that this precipitable protein is the actual antibody. This is confirmed by the recovery, from the precipitate formed by pneumococcal polysaccharide and antiserum, of a protein which is active as antibody and can be almost completely precipitated again by the polysaccharide (L. D. Felton, 1932). Breinl and Haurowitz (1930), and more recently L. F. Hewitt [6] have shown that this precipitable protein is chemically indistinguishable from serum globulin.

It is now reported that J. B. Sumner and S. F. Howell, of New York, have prepared the hæmagglutinin of the jack bean as a crystalline protein. In this form, it is stated, it caused perceptible agglutination of dog and cat red blood corpuscles in dilutions up to 1 in 10 million; on human cells it was much less effective, agglutinating them only in dilutions up to 1 in 1000. This protein, however, cannot be considered an antibody, since it occurs naturally—not in response to the stimulus of the introduction of a foreign substance; nor is there evidence that it has the specificity characteristic of most antibodies. Nor are such crystalline agglutinins a new discovery. Edestin will agglutinate sheep and human red blood corpuscles in dilutions up to 1 in 10,000, as was shown by B. White and O. T. Avery as long ago as 1913. Even tannin acting on red blood corpuscles in dilutions up to 1 in 10,000 will reproduce phenomena (agglutination, hæmolysis, complement fixation, and preparation for phagocytosis) resembling those caused by antibodies, though lacking the characteristic specificity (Reiner, 1929). Nevertheless the discovery of a pure protein agglutinin which acts in such extreme dilution may afford valuable information on the mechanism of the action of antibodies.

TUBERCULOUS MILK IN BRISTOL

In another column Prof. R. H. Parry and Prof. I. Walker Hall, respectively medical officer of health for Bristol and director of the preventive medicine laboratories, tell us of the infected farms in the area from which Bristol draws its milk-supply and which act as reservoirs for the dissemination of bovine tubercle bacilli. Last year 5 per cent. of 485 samples of milk from one area were found to contain virulent bacilli, but it proved possible to track the infection down to 14 farms, the milk from which was intermittently tuberculous over several months. It would indeed have been an achievement if these 14 reservoirs of infection could have promptly been cleared, but the inevitable delay in procedure, of which several striking examples are given, resulted in the supply in one case of known tuberculous milk for three months or more before clearance and the distribution of the herd took place. In two cases the supply was still infected after six months. Profs. Parry and Hall suggest lines of action which would lead to more effective protection of the community and are prepared to justify them as less disturbing to economic conditions than is routine tuberculin testing. That is not the only direction in which Bristol looks for progress. The efforts made in recent years to educate the farmer and dairyman in the production of milk have borne fruit in a uniformly improved standard. This fact is not however widely enough appreciated, for only a few consumers have followed the developments in the industry. The introduction by the Marketing Board of the "milk in school" scheme now offers an opportunity for the diffusion of this information via the school-children to the general public. The preventive medicine and agricultural advisory departments of the University of Bristol are accordingly providing a course of lecture-demonstrations for school teachers on such subjects as production, nutrient values, health and disease in the cow, and the means of increasing the safety of milk and storage of food. Accompanying the syllabus is a brochure on milk as a food, written in simple language as a lesson for children under 12 years, with a supplement for those over 12 years. The children are invited to write essays or make drawings, suitable for posters, upon the subject "A Glass of Milk," and prizes will be awarded to senior and junior boys and girls. The Bristol education committee is coöperating in all these arrangements.

AGRANULOCYTOSIS

In the last few years there have been many reviews and reports of cases of the peculiar syndrome commonly known as agranulocytic angina, agranulocytosis, or malignant neutropenia. (Since a sore-throat and mouth, though often, is not always associated with this condition, probably the two last names are preferable.) Dr. E. W. Adams has now reviewed "certain aspects" of this syndrome in a report issued by the Ministry of Health.[1] He emphasises the value of pentose nucleotide in the treatment and the importance of amidopyrin in the ætiology. Certain of his statements—some of them lacking exact references—are hardly in agreement with the authoritative review of Jackson and Parker,[2] who have had extensive experience of the disease. Dr. Adams, for example, says that it may occur in children, though they are definitely of opinion that no authentic case has been seen under the age of ten. He also states that the total white cell count is not necessarily lowered, whereas Jackson and Parker and the majority of other workers agree that leucopenia is a sine qua non of the syndrome. In writing on the ætiology of the disease, Dr. Adams does not mention any of the papers describing the pathological findings in hæmopoietic tissues; he is content with the statement under the heading of clinical features, that "after death the bone-marrow is found to be destitute or almost destitute of granulocytes." Many observers, however, have shown that at least in patients dying in the early stage of the disease, though mature polymorphs may be absent, there may be an excess of stem cells; and it was this finding that led FitzHugh and Krumbhaar [3] to make the important suggestion that an arrest of maturation at this level is a key to the ætiology of

[3] Marrack, J.: Med. Research Council, Spec. Rep Ser. No. 194, 1934, p. 52.
[4] Dean, H. R., Taylor, G. L., and Adair, M. E.: Jour. of Hyg., 1935, xxxv., 69.
[5] Heidelberger, M., and Kabat, E. A.: Jour. Exp. Med., 1934, lx., 643.
[6] Hewitt, L. F.: Biochem. Jour., 1934, xxviii., 2080.

[1] Min. of Health Rep. on Public Health and Med. Subjects, No. 76. London: H.M. Stationery Office. 1935. Pp. 21. 6d.
[2] Jackson, H., Jr., and Parker, F.: New England Jour. Med., 1935, ccxii., 137.
[3] FitzHugh, T., Jr., and Krumbhaar, E. B.: Amer. Jour. Med. Sci., 1932, clxxxiii., 104.

the condition. Later in the disease plasma cells and lymphocytes largely replace the previously existing stem cells.

Dr Adams supplies a useful appendix containing a list of preparations known to contain amidopyrin, which in view of the evidence he marshals must be considered a dangerous drug. Some of the listed preparations are recognised hypnotics; others are advertised pick-me-ups likely to be bought without a doctor's prescription.

POUL EDVARD POULSSON

THE death of Prof. Poulsson on March 19th removes an outstanding figure from the world of pharmacology. His text-book, originally published in Norwegian, has been translated into many languages and has enjoyed a popularity remarkable for a translated work. In many, if not most subjects, the Norwegian medical student depends on English, French, and German text-books. But in pharmacology this state of affairs was reversed, and Norway not only has its own text-book on pharmacology, but also the satisfaction of seeing it accepted as a standard work elsewhere. Poulsson was born on April 18th, 1858. After holding various internships at home, he spent three years abroad, studying chemistry under Fresenius in Wiesbaden and pharmacology under Schmiedeberg in Strasbourg. He began to lecture on pharmacology at the University of Christiania in 1891, and four years later was appointed to the chair. In 1928 he retired from this post on reaching the age limit, but he continued active in research till the end, and some of his most valuable work was done quite recently in connexion with vitamins and cod-liver oil at the State Vitamin Institute. Poulsson was also an excellent clinician, and in his early years was the chief medical officer of the Sandfjord hydro. The popularity he enjoyed as much among medical students at home as with fellow scientists at international meetings abroad depended largely on the lucidity of his intellect and his quick grasp of the essentials of any problem with which he was faced. Herein also lay the success of his great text-book which gave the reader the colour and perspective which students do not always find in the writings of their teachers. Poulsson infused some of the same qualities into his lectures. The attention of his listeners was always held by the hope, amounting almost to a conviction, that a flash of wit would give the dead leaves of pharmacology life and substance.

BRITISH ASSOCIATION MEETING AT NORWICH

FOR the second time in its history the British Association for the Advancement of Science is to meet at Norwich, this time under the presidency of Prof. W. W. Watts, who at 8.30 P.M. on Wednesday, Sept. 4th will deliver an address on Form, Drift, and Rhythm of the Continents. The previous meeting was held there in 1868 under the presidency of Dr. J. D. Hooker, botanist and traveller. Sectional addresses will be given during the week that follows by Sir Arthur Smith Woodward (Anthropology) on Recent Progress in the Study of Early Man, by Prof. P. T. Herring (Physiology) on the Pituitary Body and the Diencephalon, and by Dr. Ll. Wynn Jones (Psychology) on Personality and Age. Evening discourses will be delivered by Dr. S. J. Davies on Diesel Engines and by Dr. C. S. Myers on The Help of Psychology in the Choice of a Career. Norwich, although no longer as it was in the Tudor period the second city in the Kingdom, is still the largest city in a purely agricultural district embracing three counties, with a culture and opinion of its own in various branches of art and literature. It is still the "city of gardens" and the new town hall in course of erection is evidence of continued enterprise. There will thus be an agreeable and stimulating background for the meeting. The local hon. secretary is Mr. H. P. Gowen, F.S.A., J.P. General inquiries should be addressed to the Secretary at Burlington House, London, W.1.

THE PITUITARY AGAIN

ON another page of this issue Prof. E. C. Dodds and his collaborators at the Middlesex Hospital describe how they have produced chronic gastric ulcers in animals by means of a pituitary extract. Never before, they believe, have such ulcers been caused by injecting an extract of a normal tissue, and they give reasons for thinking that the apparently large doses given represent no more than an exaggeration of a natural process. If the observations ended here they would be sufficiently striking; but it also appears that the same extract will produce in rabbits a severe anæmia not unlike the pernicious anæmia of human beings. This leads them on to the question whether there is not some hormonal connexion between the posterior lobe of the pituitary gland, the blood picture, and the stomach.

LEARNED EXHIBITS

AT the Conversazione of the Royal Society held at Burlington House on May 3rd there were many exhibits of interest to clinicians. It is impossible to imagine any demonstration that medical science could provide in which essentially physical or chemical methods and apparatus would not play a prominent part. The exhibits of chief medical interest fall into three groups. There are (1) those which have resulted from an approach to some purely medical problem by physical means, (2) those in which medicine has appropriated to its own ends methods and apparatus designed primarily for other purposes, and (3) perhaps of greatest interest, those which give promise of providing clinical science in the near future with new or more refined methods of diagnosis or treatment.

In the first group stand the cathode ray electrocardiograph and the system of cineradiography. The former makes use of a fluorescent screen as the recording element; this has a long after-glow so that the light-accommodated eye is able to view and to examine the completed record for 10 to 12 seconds before it fades. The latter is simple enough to be available as a routine method of examination in the ordinary hospital department; the earlier drawback of prolonged and possibly excessive irradiation of the patient during the taking of a series of exposures has been eliminated by arranging for the X ray tube to be energised intermittently—i.e., each time the camera shutter opens. In the second group we find the ultra short-wave oscillators working on wave-lengths between 2·5 and 6 metres, shown by the General Electric Company. The heating effect of their discharge on several litres of dilute salt solution was demonstrated; they are suitable for medical diathermy and provide a means of generating heat in the deeply placed tissues and organs of the body without immoderately increasing the surface temperature. In the third group may be included a method of continuously measuring small traces of contaminant in a given gas; the ability which it provides of detecting the presence of heavy vapours like hydrocarbons in concentrations of only 1 : 100,000 parts of air may have most valuable applications in the field of

industrial hygiene. The use of phenolic and basic synthetic resins for the purification of water was demonstrated; they reduced both acidic and basic dyestuffs to insignificant traces, and they removed completely all the saline contents of sea water to give drinking water.

In a lecture on Dr. Robert Hooke, F.R.S., Mr. Walter Adams reminded us that July 18th of this year is the tercentenary of his birth. Side by side in another room were demonstrated Hooke's own microscope and the earliest existing photograph, taken just 100 years ago, by Fox Talbot. These two centenary exhibits are the original products of developments in physics and in chemistry to which clinical medicine owes more than can be summarised and without which medical science would be non-existent. It would perhaps have emphasised their importance and certainly have added to their dramatic value to have shown alongside these two early exhibits of photography and microscopy the two latest developments of photomicroscopy which were demonstrated: an apparatus for making stereo-micro-photographs and a twin film polygraph and strobograph for recording the very rapid and fugitive movements of the smallest animalculæ. Dr. Adrian's demonstration of the Berger rhythm aroused great interest. Using himself as the experimental subject, the resting rhythm was clearly and regularly seen after projection of the oscillograph tracing on a large screen by means of an epidiascope; the abolition of this rhythm brought about by visual stimulation, by mental effort of an unusual degree, and by unexpected cutaneous stimulation occurred regularly. The results so far achieved have been already commented upon (see THE LANCET, Jan. 12th, p. 96), but although no new results were communicated or demonstrated Dr. Adrian provided a model demonstration with an adequate and very clear introduction.

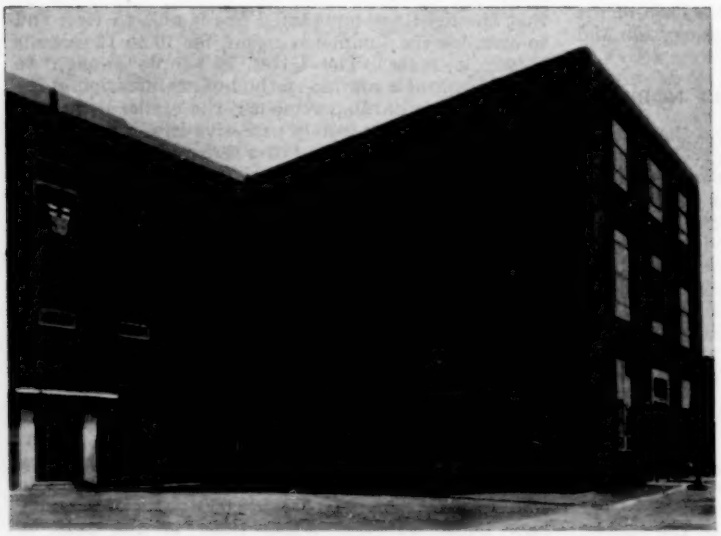
Another popular exhibit was that of some apparatus used in research into the psychological and physiological qualities necessary in motor drivers. The subject examined sits in a small motor-car, hanging in front of which is a screen upon which a cinematograph film of a model landscape is projected; the normal controls of the car control the position of this landscape on the screen and its apparent rate of approach. Movements of the car in relation to the surface of the road depicted in the landscape are automatically recorded, and from this record may be obtained a measurement of the reaction times of the driver when faced with different problems in car management. Since the time factor is one which enters so largely into intelligence testing and other forms of examination for mental ability, it seems likely that this form of test could be adapted to problems less specialised than that of car driving and might be made the basis of assessing vocational ability along many different lines.

Sir Edmund Spriggs will deliver the Croonian lectures of the Royal College of Physicians on May 14th, 16th, and 21st. His subject will be a Clinical Study of Headaches. The lectures will take place at the College at 5 P.M., and any member of the medical profession will be admitted on presentation of his card.

Surg.-Captain Sheldon F. Dudley took up his duty on May 1st as deputy director-general of the Royal Navy from the R.N. Hospital at Chatham. He was formerly director of medical studies and professor of hygiene, pathology, and tropical diseases at the R.N. College, Greenwich. In his Milroy lectures delivered in 1931, he drew some lessons of the distribution of infectious diseases in the Royal Navy; his success in limiting the spread of infectious disease at Greenwich Hospital School is common knowledge.

SOCIETY OF PUBLIC ANALYSTS.—At a meeting of this society held in London on May 1st, Dr. G. Roche Lynch and Mr. R. H. Slater, D.Sc., described a putrefaction product of toxicological significance. A crystalline para-phenylpropionic acid was formed by anaerobic putrefaction in a body which had been buried in an unsealed lead coffin, and had consequently lain for a considerable time under water without exposure to the air. This compound was extracted with ether from the acid aqueous liquid obtained in the Stas-Otoo process, and until its identity was established it was suggestive of the presence of one of the barbituric acid derivatives. Dr. Roche Lynch and Dr. Slater also reported on the toxicological examination in a fatal case of poisoning by meta fuel.

BRITISH POSTGRADUATE MEDICAL SCHOOL



THE accompanying photograph shows the entrance to the new out-patient department of the Hammersmith Hospital of the London County Council attached to the British Postgraduate Medical School, which is to be opened by H.M. the King on Monday next. The block of buildings, comprising school and out-patient department, makes up the east wing of a teaching hospital of 400 beds which is to be devoted solely to post-graduate medical education. Chairs of medicine, surgery, midwifery, and pathology in London University have been established at the school. In a recent issue (THE LANCET, April 7th, 1934) we reproduced detailed plans of the medical school and of the new surgical and maternity block, and we propose to give in an early issue an illustrated account of the equipment and system of teaching at the school.

PROGNOSIS

A Series of Signed Articles contributed by invitation

LI.—THE PROGNOSIS OF TABES DORSALIS

IT is well to regard the prognosis of tabes from two aspects: (1) as regards life, and (2) as regards incapacity.

Expectation of life.—The disease is compatible with 20 or more years of life and thus, in favourable circumstances, need not affect the expectation of life of its victim. Where, however, the original infection has been severe, if tabes develops at all, the interval between infection and development is likely to be short (in years) and the duration of life in such a case will be much less than the average for tabes.

It is significant that while the death-rate from syphilis (per 1000 live births) under one year of age has now fallen to roughly one-third of its pre-war level, and the death-rate from general paralysis has been halved in the same period, doubtless owing to modern therapeutic measures, the death-rate from tabes still remains much where it was; it now averages about 19 per million of the population, as against 21 before the war. The incidence of tabes in men is about ten times what it is in women. About 10 per cent. of syphilitics develop nerve syphilis, and less than half of these are tabetics. There will be general agreement that the incidence of tabes has been reduced in recent years, but as the duration of the disease so greatly exceeds that of general paresis, the death-rate takes much longer to show an improvement.

Incapacity.—The form of incapacity varies—all the disabling features are not found concentrated in any one case, however severe the infection may have been in the first place. The two main groups of disability are those affecting (*a*) eyesight, and (*b*) locomotion. It is noteworthy that even a definite optic atrophy may be stayed in its progress if detected early, and efficient treatment in the nick of time may save for the patient at least a modicum of vision.

IMPORTANCE OF EARLY DIAGNOSIS

The outlook in a given case of tabes dorsalis depends very largely upon an early diagnosis, followed by efficient and vigilant treatment. Thus much depends on the intelligent interpretation of a suggestive sign or symptom—it may be shooting pains, a perforating ulcer under one great toe, a difficulty in beginning to urinate, the presence of cystitis, the sudden appearance of a squint, or the accidental discovery of a single sluggish pupil or of unequal pupils. The prognosis of the individual case depends on whether full investigation and intensive treatment follow immediately. On the other hand, a diagnosis of tabes must not be accepted without verification. Many of us have been told that knee-jerks are absent when they are in fact present, albeit difficult to obtain. In this connexion it should be remembered that ankle-jerks are always lost first, and if they are retained in any case the apparent absence of knee-jerks need not cause alarm.

ARREST IN ADVANCED CASES

It is often stated that a case of tabes should never be allowed to reach the ataxic stage. This is true, but should not be taken to mean that if ataxia has begun to show itself treatment will certainly not be effective. Except in those rapid cases which follow a year or two after the original infection, where the prognosis is always hopeless, there is a good chance of improvement even when ataxia is manifest. But no treatment can benefit a blindness, already absolute, from optic atrophy, though I have under my observation at the moment a woman in whom the progress of the atrophy has been stayed and some degree of vision preserved following efficient treatment. I have had more than one case in which a single Argyll Robertson pupil has again become reactive to light. There are suggestions that the optic atrophy case just referred to may become mental, a point which suggests the necessity of bearing in mind the fact that tabetic psychoses occur as well as taboparesis; and the prognosis of the one is very different from the prognosis of the other. Just as a "leg" tabes will not go blind, so, as a general rule, an "optic" tabes will not later develop any ataxia. There is no stage in any case of tabes at which "arrest" may not occur. If, as I have said above, early onset of tabetic symptoms after infection means as a rule a rapid course, late onset, always presuming that we can exclude taboparesis, means a slow one. But in these cases expectation of life must to some extent differ with social status. A poor patient cannot so easily maintain his general condition, so as to prevent intercurrent infection, as can a prosperous one. Ascending infections of the genito-urinary tract make quicker headway and occur more often in the poorer type of patient. A well-to-do man with "leg" tabes may, as is well known, go about for years in a wheel chair, mentally very alert, beating everyone at bridge, and having no other disability save that of locomotion.

RE-EDUCATION: CRISES

There is no limit to the duration of the pre-ataxic stage, and some cases never go beyond it. Here re-education may work wonders in postponing or preventing the onset of developed ataxia. The various crises are never fatal at the time, and it has been said that they do nothing to shorten life. This has not been my experience. In some, crises seemed to herald an advance of the disease; in others the general resistance to infection had been so diminished that an ascending urinary infection was soon fatal. This was so, for instance, in one man with gastric crises which failed to respond to chloretone; morphia had to be given, eventually in very large doses, and for so long that debility and cachexia became pronounced. Another of my intestinal crises cases, having survived the attentions of a surgeon who had treated him as an acute abdomen, and having got through subsequent attacks aided by medical treatment, in the end died of apoplexy. An elderly patient becoming bedridden as the result of the collapse of a limb following a Charcot's joint may soon die from extensive bedsores, and the same result may occur where a case of tabes is associated with a fracture due to fragilitas ossium. Evidence of syphilitic aortitis is not a discouraging feature.

URINARY INFECTION

A rule of treatment upon which the individual prognosis depends more perhaps than any other is regular testing of urine and examination for retention with overflow. The patient may not complain of

discomfort and one may have no idea that any urinary trouble has begun. But unless the condition is discovered early and efficiently treated, urinary infection takes place and the patient goes downhill rapidly. In the same way severe bone disease and foot sepsis may occur before a perforating ulcer, being anæsthetic, has been noticed.

LABORATORY FINDINGS

The inferences one is justified in drawing from laboratory findings as regards prognosis deserve notice. In a doubtful case the assurance that the blood Wassermann is negative is not enough. We must be sure that there is no pleocytosis of the cerebro-spinal fluid, for this is a constant and a very early sign of tabes. The cerebro-spinal Wassermann is positive in over 75 per cent. of cases if 1 c.cm. of fluid is used; this is a rather larger figure than the percentage of blood-positive Wassermanns. An early change to negative under treatment is of good omen. A diminution in the lymphocyte count of the cerebro-spinal fluid under treatment is also a good sign, and is the easiest change in laboratory findings to obtain; whilst a high pre-treatment count suggests that treatment is worth while and prognosis relatively good. A diminution of cerebro-spinal protein under treatment is a favourable sign. The globulin, however, is much less likely to alter under treatment. A colloidal gold curve which is luetic in type (0 0 1 4 3 2 0 0 0 0) is also favourable, a paretic curve (5 5 5 5 4 4 3 2 0 0) being of course the reverse. Where arrest takes place there may be no curve, and the cerebro-spinal fluid may become normal again. It must be remembered, however, that even in a tabes which is clinically advancing the blood and even the cerebro-spinal fluid may come to yield and to continue to yield a negative Wassermann. If either or both (blood and fluid) become negative in a case in which they have been previously positive six-monthly tests must be done, and the signs and symptoms must always be regarded as over-riding any tests from the point of view of prognosis.

TABOPARESIS

It is absurd to assume that because a patient with tabes does not at the onset suggest taboparesis he will never at any time develop paretic symptoms. If such symptoms do appear then, even with malarial treatment, which is not so successful here as in ordinary general paresis, the patient is not likely to survive more than, at the most, four years. It is just as important to be on the look-out for the development of taboparesis as it is to watch for urinary infection, pulmonary tuberculosis, influenza, or pneumonia, any of which may be insidious in onset or development. The full examination of the cerebro-spinal fluid may here be the only sure guide.

The warning not to confuse psychoses with taboparesis has already been given. Juvenile tabes progresses fast if it develops early, slowly if it comes on late, unless it is aggravated in its progress by an acute infection or by an accident. Similarly with conjugal tabes. It is just as worth while to treat juvenile tabes efficiently as it is the adult form. Alcoholic tabetics do badly, and the disease progresses rapidly.

In all forms and at all ages the maintenance of the general condition is of cardinal importance to the prognosis. Next to this comes the success with which re-education can be achieved.

FRANK E. TYLECOTE, M.D. Viet., F.R.C.P. Lond.,
Hon. Physician to the Manchester Royal Infirmary, and Professor of Systematic Medicine in the University of Manchester.

SPECIAL ARTICLES

EPIDEMIC INFLUENZA: A VIRUS DISEASE *

BY P. P. LAIDLAW, F.R.C.P. Lond., F.R.S.

INFLUENZA is one of the greater scourges of mankind. In epidemic form, on many occasions, it has spread throughout the world causing incalculable damage. For example, the pandemic of 1918–19 is estimated to have involved 500,000,000 people and cost the world upwards of 15,000,000 lives. Previous to this (e.g., 1889–90 and 1836–37) other pandemics of corresponding magnitude had taken their toll of humanity. Between the great pandemics, often following them closely, lesser outbreaks have occurred from time to time, involving a country or a part of it, a barracks or a school. In addition to these patches of localised infection there are sporadic cases of disease which are often diagnosed as influenza; but we have no assurance that these sporadic cases are really the same disease and have the same ætiology as the epidemic cases. It is, in fact, very doubtful if they always are, and I, for one, feel that many of these cases would be better labelled with the old war-time diagnosis, honest if non-committal, P.U.O., or pyrexia of unknown origin. Further, we have no proof that the different epidemics are due to one and the same cause; there are indeed difficulties in the way of accepting this view literally. Yet there is such great similarity in the spread of the disease and the symptoms recorded for different epidemics and pandemics that it seems fairly certain that if there are multiple causal agents these must be close relatives and connected in some way.

Epidemic influenza is characterised by great infectivity with rapid spread in a population, a short incubation period of about 48 hours, a very sudden onset with fever, malaise, and depression, passing on to prostration. Pains in the head, back, or limbs are common. A coryza and some pharyngitis can usually be detected. After a few days' fever, in the majority of cases, recovery sets in and the temperature subsides to normal; but there is left behind a condition of depression and weakness quite unexpected in view of the short period of fever and the slight physical signs. In a proportion of cases tracheitis, bronchitis, and broncho-pneumonia may develop when the mortality-rate rises steeply. During an epidemic the diagnosis is relatively easy, for many severe as well as mild cases are seen; and all stages of the disease may be observed on one day. There is, moreover, ample evidence of great infectivity. But in sporadic cases where evidence of infectivity is lacking and the symptoms are often milder it may be impossible to reach a sure diagnosis. Again, at the beginning of an epidemic or in the early stages of the disease, it may be very difficult to diagnose a case with confidence.

It is not the province of a pathologist to discuss the clinical aspects of the disease or to lay down

* The Linacre lecture of St. John's College, delivered at Cambridge on May 7th, 1935.

rules by which the diagnosis of influenza will be justified, though it may be permitted him to point out certain difficulties and plead for a more refined and intensive clinical analysis of cases of the influenza type. I propose rather to consider here certain experimental facts which have been accumulated during the last three years, and which appear to me to show that it should become possible in the future to separate with precision epidemic influenza from other diseases which simulate it.

It is clear that if the cause or causes of influenza could be identified with certainty a great step would have been made in this direction, and I believe it is now being gradually proved that the *primary* infective agent in epidemic influenza is a filtrable virus. It is with this aspect of the subject that I propose to deal. It must not be supposed that the bacteria which have been cultivated from cases of influenza are of no significance in the human disease. There is a great deal of evidence which shows that the visible bacteria are very important in particular cases, and it should be stated that Pfeiffer's bacillus or *Hæmophilus influenzæ* is still regarded by many observers as the prime cause of the disease and many of its complications. I shall not go into this question in detail, but if a virus is proved to be present in the early stages of influenza infection it seems to me that the visible bacteria, including Pfeiffer's bacillus, must be regarded as secondary invaders of tissues damaged by the action of the virus.

The Virus Hypothesis

It was suggested about 1914 that influenza was really a virus disease. At that time knowledge of viruses was meagre, and although we know much more to-day about virus diseases we do not yet know a great deal about the viruses themselves. The view with the greatest following at present is that viruses are exceedingly small micro-organisms with very strict parasitic habits. The small particles which can be demonstrated in suspensions of viruses are so minute that special methods are required for their elucidation, but it does seem that we are gradually getting to know something of the shape and form of virus particles. The parasitism of many viruses is so strict that they will only grow in one or two species, and sometimes show a striking preference for certain tissues of the host. They cannot be cultivated, with perhaps one or two exceptions, on artificial media apart from living cells.

The virus hypothesis for influenza postulated, therefore, that the infective agent was so small that it could be separated from visible micro-organisms by filtration, that it was most probably an obligate parasite incapable of growth except in the animal body and that the parasitism might possibly be so strict that it would grow and cause disease only in man.

This hypothesis became prominent during the pandemic of 1918–19, for at that time a number of workers ventured to question the claims of *H. influenzæ* to the rôle of principal villain in the drama of influenza, although this organism had held an almost undisputed position since the end of the pandemic 1889–90. There was not much experimental evidence in favour of the virus theory at this time because no one knew of an experimental animal which was susceptible to infection with human influenza. Recourse was therefore made to human volunteers. Nicolle and Lebailly (1918) and de la Rivière (1918) record what appeared to be successful infections with bacteria-free filtrates of material from influenza patients. Yamanouchi, Iwashima, and Sakakami also appeared to be successful in a larger series of experiments. But against these must be placed the negative results of MacCoy, Rosenau, and others (1921), Friedberger and Konitzer (1919), Lister and Taylor (1919). All these experiments on human volunteers are of very doubtful value. Man is an exceedingly bad experimental animal and almost useless when he is used for experiment during an epidemic. One can never be sure that the experimental subject is susceptible and therefore negative results can be discounted; while positive results, though perhaps more significant, are always open to the suspicion that infection was picked up in some accidental manner. On the other hand, in the absence of an epidemic there is no supply of virus to test on presumably susceptible subjects.

The Ferret Susceptible to Influenza

In 1933 Smith, Andrewes, and I began to hope that we had discovered a method of studying influenza in laboratory animals. We found that it was possible to transmit a disease to ferrets by inoculating intranasally filtrates of pharyngeal washings from cases of epidemic influenza in man. The filters we employed were Gradocol membrane filters made and supplied by our colleague, Dr. Elford. They had an average pore size sufficiently small to keep back all visible bacteria, and as far as we could determine, the filtrates we used were bacteriologically sterile. We obtained 5 successful transfers from 8 cases of "influenza" and then the epidemic disappeared. Subsequent to this, throat-washings from sporadic cases diagnosed as influenza and from normal subjects failed to infect ferrets, and nasal secretions from cases of "common cold" were also without effect. The disease in the ferrets was of varying severity and would pass from a sick animal to a healthy one by simple contact, in other words the experimental disease was contagious.

Isolation of experimental ferrets.—Experience with dog distemper had shown us that somewhat elaborate precautions were necessary to prevent the accidental spread of any highly infectious disease, and we immediately adopted the scheme of rigid isolation which was evolved for the work on dog distemper.

The plan is to house all experimental animals in a special building which can only be entered through a passageway, the floor of which is constantly covered with a lysol bath three inches deep. All workers therefore wear rubber boots and rubber overcoats. On entry into the building boots and coats are washed down with lysol. There is a central hall round which are a number of cubicles, each of which is completely separated from the others and from the central hall. Each experimental ferret is placed in a special cage and the cage in a cubicle. Before entry into a cubicle the worker or attendant is swabbed down with lysol so that any infectious material, dust, sprayed droplets, &c., sticks to the damp surface and is subsequently sterilised by the lysol wash which follows on emergence from the cubicle.

A routine of this kind is very irksome and it slows down the work enormously, but if the ritual is carried out faithfully we can be confident that the experimental animals are safe from accidental cross-infection from one to another. In addition to being cumbrous the method is costly, for a special building is required and a reliable staff of attendants. Lack of adequate accommodation such as we desired compelled us to abandon some of our original strains and work more intensively with one in particular. This strain was recovered from one of the team (W. S.) who contracted influenza soon after the investigation was under weigh. There is no proof, but it is quite possible

that he became infected from the experimental animals. It is suggestive that his illness developed at a time when the epidemic had almost disappeared and chances of outside infection seem to have been remote.

The virus.—The infecting principle is abundant in the nasal mucosa of sick ferrets, and for routine supplies of virus the diseased mucous membrane is ground in a mortar, emulsified with saline, and the resultant suspension is centrifugalised. The opalescent supernatant fluid is rich in virus and contains small numbers of visible bacteria, which may be eliminated if desired by filtration through a suitable membrane filter. Infective filtrates have been specially examined for the small filter-passing organism *Bacterium pneumosintes* of Olitsky and Gates (1921) because this small organism was believed by the two discoverers to be the primary infective agent of influenza. We have never encountered it. Inoculation of culture media, suitable for the multiplication of *B. pneumosintes* with our virus followed by incubation, results in total loss of infectivity. The virus has, in fact, not yet been cultivated on artificial media. It is destroyed by heating to 56° C. for an hour and it will withstand drying or storage in glycerol for many weeks.

A remarkable feature of this virus is the fact that it will only infect through the respiratory tract. Subcutaneous, intravenous, intraperitoneal, or intracerebral inoculations are without effect. Again, the virus can only be recovered from the respiratory passages or lungs. Blood, cerebro-spinal fluid, liver, spleen, and brain do not appear to contain any virus, even at the height of the disease.

The facts are very remarkable. Virus can be recovered only from the nasal mucosa and the lungs which are, after all, surface structures; it cannot be recovered from the deeper tissues. Yet it is clear that the virus or its products does invade the body, as is shown by the symptoms of disease and the production of circulating antibodies. What may be the explanation of the facts we do not know, but they help to differentiate the virus from others, and they must be taken into account when considering the full explanation of the disease.

Influenza in the ferret.—The virus disease in the ferret is characterised by an incubation period of about 48 hours followed by fever in which the temperature may reach 107° F. This is followed by a remission and thereafter a second febrile period usually lasting three or four days, during which there are symptoms of nasal catarrh, such as sneezing, nasal obstruction, mucopurulent discharge from the nose, and sticky accumulations round the nares. Throughout the illness, but varying greatly from case to case, there is prostration and occasionally signs of muscular weakness. The disease is never fatal when ferrets are inoculated without an anæsthetic. Certain strains of streptococci in conjunction with the virus do produce a more severe disease and prolong the illness, but do not cause a fatal outcome. Hæmophilic organisms from ferret, pig, or human beings do not appear to modify the disease materially.

When the intranasal instillation of virus is made, in series, into ferrets which are anæsthetised with ether (Shope, 1934) pneumonia develops in the inoculated animals. Without an anæsthetic the recently isolated human strain of virus never causes pneumonia, but after passage through many ferrets pneumonia may occur. The cut surface of the solid lung is usually bacteriologically sterile, and emulsions of solid lung, though rich in virus, are usually free from bacteria, and there is no doubt that the virus by itself can, and on occasions does, cause a characteristic pneumonia.

Sections of the nasal mucosa, from ferrets killed in the later stages of the disease, always show signs of acute inflammation, vascular engorgement, dilated lymph channels, catarrh of the superficial epithelium, loss of all ciliated cells, and collections of mucopurulent exudate in the air spaces. Many polymorphonuclear leucocytes can be seen on their way through the remains of the epithelium. Inclusion bodies have not been detected.

Immunity.—Ferrets which have recovered from an attack of the disease are immune to further infection for a few months, but after six or seven months they gradually become susceptible once more. Reinfection at about this time leads to a sharp febrile attack with the usual symptoms of the primary attack, but the second attack is usually milder and of shorter duration than the first.

Serum from a convalescent ferret contains antibodies to the virus. These may be demonstrated by mixing virus and serum together and allowing the mixture to stand at room temperature for ten minutes and then instilling the mixture into another ferret's nostrils. Normal ferret serum has no neutralising power. Convalescent human serum, and in fact most human sera, also contains antibodies for the virus; indeed, we have only found two human sera which fail to neutralise when mixed with virus. It has been found to be possible to prepare antiserum in bulk by oft-repeated subcutaneous injection of virus into horses and to demonstrate its potency by admixture of serum with virus as just described for ferret serum.

Influenza in Mice

In 1934 we discovered that the virus from ferrets could be adapted to mice. This means that it was found possible to infect mice when ferret virus was instilled into the nostrils of mice which had previously been anæsthetised with ether. In the first group of mice so treated only a small proportion showed signs of infection. Inoculations with material from the sick mice to others, however, led to more regular infection and a more serious disease. After several transfers the virus infected nearly 100 per cent. of mice and induced an illness which was very often fatal. The disease in mice is essentially a pneumonia which spreads from the larger bronchi to the periphery of the lung, and in fatal cases the process results in almost complete hepatisation of the lungs.

I do not propose to enter into a consideration of the histological changes which are to be found in the pneumonic lung. For our present purpose it is sufficient to point out that the cut surface of the solid lung is usually sterile, and that small fragments of solid lung, on incubation in culture media, often show no growth of visible bacteria. The organisms which are occasionally encountered are of different types and can have no causal relationship to the disease process, since they can be filtered off and typical infection produced by the filtrates. In the mouse, then, as in the ferret, pneumonia may be produced by the virus, and in the mouse this pneumonia is frequently fatal.

The upper parts of the respiratory tract of mice do not seem to be susceptible to attack by the virus as is the case in the ferret. The nasal mucosa, for example, appears to be unaffected even in fatal cases. Corresponding with this there is no sneezing, and as mice do not cough dissemination of the disease does not occur. It is thus possible to conduct experiments on mice without the elaborate isolation precautions

which are advisable with ferrets and, in our experience, if simple precautions are taken as to cleanliness, cross-infection from one group of mice to another does not take place. Unfortunately the mouse does not appear to be as susceptible as the ferret and, so far as our experience goes, it has not been found possible to infect mice directly with human material. If it were possible to dispense with ferrets future work would be greatly simplified. Again in the case of mice, as has already been described for the ferret, it is only possible to infect by the respiratory tract, and the only tissue from which virus has been recovered in mice is the diseased tissue—namely, the lung.

Neutralisation of mouse virus by means of antiserum can be demonstrated and we have found it possible to assess the potency of a serum by determining the lowest dilution of a serum in a mixture of serum and virus which would neutralise all virus.

We thus obtained in 1933 from cases of influenza in man a virus which produced characteristic diseases in both ferrets and mice, and for which specific antisera could be prepared. The virus could be stored in dry form or maintained in full activity by serial passage in animals, and we felt confident that with the information we had regarding the disease produced by the virus, its properties and the neutralising serum at our command, we could determine whether a virus, from some other source or from some new epidemic, was identical with the original strain or different.

Recent Experiences with Influenza Virus

Experience in 1934.—We fully expected to obtain new strains of virus in the winter 1933–34, but, as time passed, our hopes were disappointed, for there was no widespread epidemic of influenza in London and we did not obtain any material from cases of the true epidemic type. Sporadic cases diagnosed as influenza were tested on several occasions but from these, as was also the case the previous year, we did not recover any virus. In March, 1934, we obtained material from a patient in a household of five, every member of which suffered an attack of what appeared to be typical influenza. The outstanding clinical difference between this case and the sporadic ones was the evidence of high infectivity. From this case we recovered virus without any difficulty. The diseases induced in ferrets and mice seemed the same as those produced by the original strain. More important than this, however, was the fact that the original and the new strain cross-immunised. A ferret immune to the old strain was also immune to the new, and a ferret immune to the new strain was immune to the old. The horse antiserum which was made with the original virus as antigen neutralised both old and new viruses apparently with equal ease There is no doubt in our minds that the 1933 strain and the 1934 strain are essentially the same.

Experience in 1935.—During the winter 1934–35 there was no epidemic of influenza in the London neighbourhood, and we began to believe that our experience was again going to prove as disappointing as in the preceding winter. Through the kind offices of Colonel Marrian Perry of the Royal Army Medical College and the activities of the Army Medical Services, to whom we are very greatly indebted, we obtained material from cases of illness in the Army personnel diagnosed as epidemic influenza, and the results of the examination of the specimens submitted are of considerable interest. First, we were supplied with specimens from Woolwich. The Army authorities collected garglings from the most typical cases available at the time and sent them to us together with brief clinical notes. More specimens were received than could be examined with the limited accommodation at our disposal, and so 6 specimens were selected as being the most promising as judged by the clinical histories, and these were examined bacteriologically and inoculated into ferrets. No virus could be detected. This was very disappointing to us, for here was complete failure to obtain the virus we expected from illness of the epidemic type, diagnosed by the Army Medical Services as influenza. Moreover, the material had been collected early in the disease and in the manner we had suggested. It is true that there was some unavoidable delay in the collection of the specimens and the inoculation of these into ferrets, but this delay did not seem to be excessive.

Colonel Perry sent us, in the second place, a supply of specimens from Shorncliffe where influenza had been occuring for some time previously. These were dealt with as before and from 6 out of the 8 specimens selected for test we obtained virus. We breathed again.

The thorough testing of these strains against the original virus of 1933 is a slow matter and it is not yet complete, but so far as we have tested the point the strains of 1935 appear to be identical with that obtained in 1933. Ferrets which are immune to the original strain are immune to the new strains, and ferrets recovered from the new strains of virus are immune to the old. The more refined tests with specific immune serum prepared in the horse and performed on mice also show that the new and the old strains are of the same type. If any difference is demonstrated in the future I feel confident it will prove to be a minor one, and that the new and old strains are essentially the same.

The results of the examination of the specimens from Woolwich contrasted with those from Shorncliffe are most striking and some explanation of the facts is desirable. The most obvious explanation is that the two sets of specimens came from two outbreaks having a different ætiology. We were informed that the Woolwich cases were, on the whole, insidious in onset, which is quite unusual in true influenza, so that it is possible that they were really some other disease. But if this is the case it is clear that the clinical diagnosis of influenza, even during an epidemic, is a difficult matter, and finer clinical analysis of cases is highly desirable.

We received through the kind activities of Dr. G. H. Faulkner and the assistance of the authorities of Lambeth Hospital, specimens of pharyngeal washings from 4 cases diagnosed as influenza, and one specimen from a case of fatal "influenzal pneumonia." These must be classed as sporadic cases, since there was no evidence of spread from the donors to contacts. From 1 case out of the 5 (pharyngeal washings from a case of influenza 48 hours after onset) we obtained virus. This strain is also under investigation, but so far as tests go it appears to be identical with that of 1933.

A number of other sporadic cases were investigated from Guy's Hospital, St. Bartholomew's Hospital, and Hammersmith Hospital. From only one of these (a case from St. Bartholomew's Hospital) did we obtain an apparent positive result. The tests of this virus again show that it is probably identical with the original.

In 1935, then, we obtained 8 new strains of virus from two different parts of the kingdom, and they all appear to be the same as each other, and also identical with those isolated in 1934 and 1935.

American experience.—In August and September, 1934, an epidemic of respiratory infection prevailed

in Porto Rico. "In its clinical course it appeared to be typical epidemic influenza though the mortality was low." Specimens of sputum from selected cases were sent to Dr. T. Francis, Jun., of the Rockefeller Hospital in New York. During the winter of 1933–34 Francis had tried, without any success, to infect ferrets by intranasal inoculation of material from a number of diseases, including examples of the "common cold" and two cases of clinical influenza. Three of the specimens from Porto Rico were inoculated intranasally into ferrets under ether anæsthesia. On the second day after inoculation each of these three ferrets developed fever. One of the ferrets was killed on the third day, and an emulsion of the nasal mucosa and the lungs was made. The emulsion was filtered through a Berkefeld V. candle, and it was found that the bacteria-free filtrate, when inoculated intranasally, induced disease in another ferret. After the sixth passage pneumonia always developed in ferrets which were inoculated under ether anæsthesia. From Francis's description of the disease in his ferrets, the course of the fever, the symptoms, and the post-mortem appearances, there was no doubt that he was dealing with a disease very similar to that described by us in 1933. One of Francis's laboratory attendants developed clinical influenza early in the course of these researches. From the attendant Francis recovered a virus with similar properties to those shown by the Porto Rico strain, though there appeared at first to be some differences. Francis also discovered, independently, that mice could be infected with the virus from ferrets and that a fatal pneumonia might ensue.

On the whole it seemed that the Porto Rico virus was more vicious than the English one, producing more extensive lesions in the lungs of ferrets and killing mice more rapidly. We were naturally thrilled when we learned of Francis's success with an epidemic in another part of the world, and we sent him a small supply of the specific antiserum prepared in a horse. Imagine with what impatience we awaited news of the result of his tests to determine whether the Porto Rico strain was really identical with our strain or whether it would prove to be different in some way.

The results of these tests have not yet been published, though they are expected to appear in the very near future. Dr. Francis has given me permission to state that the Porto Rico strain appears to him to be identical with ours and, *further*, that the strain he secured from the Philadelphia outbreak about January, 1935, is also of the same type. Dr. Francis has also generously sent specimens of these two viruses to us, and our results, so far, are in complete agreement with his.

SUMMARY

Summarising the results to date we may say that virus has been isolated on several occasions from epidemic influenza cases in man, capable of infecting ferrets and mice and producing characteristic diseases in both species. All strains of virus are neutralised by one specific antiserum. The virus is therefore one, and it has been obtained from cases in London 1933, London 1934, Shorncliffe 1935, London 1935, Porto Rico 1934, and Philadelphia 1935. The evidence is thus accumulating rapidly in favour of the virus hypothesis. In fact it appears to me already transformed into a theorem which in the future will be capable of demonstration.

We must not, however, lose sight of the fact that much remains to be explained; the sporadic cases are a difficulty, and the collection of cases at Woolwich from which we failed to recover virus remains mysterious. It may be that we are inclined to lay too great emphasis on the negative results following inoculation of ferrets with material from cases diagnosed as influenza. Failure to infect a ferret may merely mean that there was an inadequate concentration of virus in the material collected from the patient (the total amount of virus collected by washing a mucous membrane with saline is probably small), or that such virus as was present lacked aggressiveness for ferrets. To put it in another way, it may be that man is a much more sensitive test-object than a ferret for influenza virus. If this were so the clinical diagnosis might represent the truth more nearly than the ferret test we have used. We do not know.

Further, if there is only one influenza virus, it will not be easy to account for the periodic appearance of the great pandemics which have, from time to time, spread over the world. There are probably several factors concerned in the production of epidemics and pandemics, but of these the resistance or susceptibility of a population to infection must be very important. The passage of an epidemic leaves behind the more resistant of the population; some do not contract the disease because they are resistant from the outset, others contract the disease, recover, and are probably immune for a time. Repeated epidemics of one type should result in a resistant stock. If the human population has been repeatedly and frequently exposed to infection by this particular influenza virus, it is not easy to understand how a pandemic due to the same virus can develop.

Swine Influenza

Let us turn, however, to another set of observations which have a bearing upon our main problem, though at first sight they may appear to be of smaller importance. Consider the epizoötic disease known as "hog flu," or swine influenza. Swine influenza did not occur, or perhaps was unrecognised until 1918. Dr. J. S. Koen, then an inspector in the division of hog cholera control of the Bureau of Animal Industry in the United States of America, was greatly impressed, first, by the simultaneous prevalence of human influenza and the new disease of hogs, and, secondly, by the resemblance of the symptoms seen in man to those occurring at that time in pigs. He concluded that the two diseases were the same, and gave the name of "flu" to the new disease of hogs. Koen's view did not meet with general acceptance but the name was considered suitable, and the disease has persisted intermittently ever since. It is to-day a serious disease for the farmer who raises pigs on a large scale in the United States. Dorset, McBryde, and Niles (1922) record a typical but unusually severe outbreak in a herd of 102 young pigs.

On Dec. 3rd the herd looked normal. On the 4th the farmer first noticed symptoms of sickness. "On Dec. 6th 11 had died and the entire remainder of the herd was so sick that they could be walked among and even kicked without forcing them to move." The severe state of illness remained practically unaltered until the sixth day of illness when there was a remarkable improvement, "almost all of the entire herd was up and eating." Full restoration of health and bodily condition was a slower matter. In this outbreak the mortality was about 10 per cent. It is usually about 2 per cent., though in very exceptional instances it may reach 25 per cent.

The symptoms of swine influenza are fever, when the temperature may reach 105° or 107° F., anorexia, profound prostration, apparent muscular weakness,

and perhaps muscle tenderness, cough, and a laboured jerky breathing. The duration of the disease is short, usually from 2–6 days, and apparent recovery is almost as dramatic as the onset. Fatal cases show, according to Shope (1931) "an extremely œdematous type of broncho-pneumonia."

The analogies with human epidemic influenza are very striking. In both we have high infectivity and rapid spread of the disease, short incubation period, sudden onset, high fever, prostration, muscular weakness, cough, and in fatal cases extensive pathological changes in the lungs. The ætiology of this disease remained obscure for some years, but Shope (1931, 1932) succeeded in demonstrating in a series of brilliant researches that this pig disease is a complex; and results from a dual infection with (*a*) a filtrable virus which by itself is almost harmless for pigs, and (*b*) a special hæmophilic organism, *Hæmophilus influenzæ* (*suis*), which alone is powerless. Infection with a mixture of virus and bacillus regularly produces a serious and sometimes fatal disease in susceptible pigs. Now, the filtrable virus from the pig disease will infect ferrets, as shown by Smith, Andrewes, and Laidlaw (1933), confirmed by Shope (1934), and produce in them a disease which is almost indistinguishable from the disease caused by the human strain of influenza virus. There is a similar short incubation period, the same type of fever, almost identical symptoms and precisely analogous changes in the nasal mucosa. On the whole, the porcine strain of virus seems to be more virulent and, in the earlier transmissions, possess a greater affinity for ferret lung tissue. Ferrets which are immune to one strain of virus are always resistant and sometimes immune to the other. Mice, under light ether anæsthesia, can be infected with the porcine strain and show lung lesions which are indistinguishable from those following infection with the human strain.

Immune sera can be prepared in ferrets and horses, and tests of these sera on ferrets and mice prove that the two viruses have some antigenic elements in common, but also possess different constituents.

DISCUSSION

The significance of these results is very great. Shope has proved, for the pig, that the combination of virus plus hæmophilic organism is much more potent than was to be expected from summing the mild diseases caused by the two agents acting separately. By analogy it seems highly probable that a similar state of affairs will also hold for man. Under this view the virus alone would cause the milder uncomplicated cases of influenza of short duration, which are so common during epidemics, and that dual infection with virus plus hæmophilic bacilli would be responsible for cases with complications such as sinusitis, purulent bronchitis, broncho-pneumonia, &c. If the secondary invader were varied or there were more than one, many of the remarkable bacteriological findings in cases of epidemic influenza of the past would be adequately explained. The proof or disproof of this conception of the disease in man must await intensive study of complicated cases during an epidemic.

But there is more than this to be gained from a consideration of the swine influenza virus and its activities. As we have seen, the pathogenic activities of human and porcine strains of virus are very similar for ferrets and mice. Are they similar for pigs? In 1933 my two colleagues and myself attempted to infect pigs with our 1933 strain of virus from man, but without success. Quite recently, however, Elkeles has informed us (private communication, 1935) that he has achieved successful results. He concludes: "That the virus obtained by Smith, Andrewes, and Laidlaw from influenza patients when inoculated, especially in combination with *H. influenzæ*, intranasally to young pigs, is able to produce in them clinical and pathological symptoms of a characteristic disease." The symptoms he records, and the post-mortem appearances he describes, are similar to those recorded by Shope for experimental swine influenza. If Elkeles's results could be extended to show that it was possible to produce a disease in pigs with human virus which was capable of inducing a typical epizoötic in hogs, the pathogenic similarity between the two virus diseases would be complete; but the facts as they stand are significant enough.

We have two viruses of different origin capable of causing similar diseases in three species of animals—ferrets, mice, and pigs. These two viruses have been shown to have certain similar antigenic constituents as well as certain different ones. The conclusion seems inevitable that the viruses are really close relatives, and Koen's view regarding the ætiology of "hog flu" becomes more than plausible. It seems to me, indeed, exceedingly probable that the virus of swine influenza is really the virus of the great pandemic of 1918 adapted to the pig and persisting in that species ever since. Adaptation of a virus to a new species has been accomplished experimentally again and again in virus diseases. It appears to consist merely in an alteration in the aggressiveness of the virus for the new host. This important modification of virus activity has not yet been shown to be associated with alteration in the antigenic structure of the virus. If our conclusion is justified it would mean that the virus of the 1918 pandemic, though closely allied to that now current in the human population, was really slightly different. This very difference between the two strains of virus gives us a possible explanation for the pandemic.

At some time or place a variant of the current influenza virus appeared and this variant might be expected to flourish in a population which was resistant to the parent strain. It is not quite the same thing as a new virus attacking a fully susceptible population, but if the variation were great enough the result as to spread and attack rate might approximate to this and the resulting epidemic might become world wide.

Similar arguments might be made for the other pandemics, and it is quite possible that all pandemics may be due to the occurrence of variants of one type of original virus. The argument is highly speculative but plausible. Proof could only be obtained from an intensive study of viruses from many epidemics and pandemics, and comparing the properties of viruses which are isolated from time to time and place to place. Some further light may come on this question from the work now in progress by my two colleagues on the antibody content of human serum against the human and porcine strains of virus, for the antibody content of a serum may be taken to indicate the past history of the donor and whether he has been exposed to a given infection or not. The future must decide whether the results prove valuable.

I have tried to indicate the lines of work and some of the results which emerge from the modern study of epidemic influenza, and to give grounds for my conviction that the primary infective agent in this disease is a filterable virus, and, further, to show that there is room for an adequate explanation of the pandemics as well as the epidemics under the virus theory.

In conclusion, I should like to make special recognition of the work of Drs. Shope and Francis in the United States, and that of my two colleagues Drs. Andrewes and Wilson Smith in this country, for with the enthusiasm of youth they have all performed a great many experiments in a limited time, often under adverse conditions, and they have been prepared to question everything if by so doing fact and theory could ultimately be brought into greater harmony.

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PARIS

(FROM OUR OWN CORRESPONDENT)

DUPUYTREN

THE centenary of Guillaume Dupuytren, who died in 1835, was recently celebrated at the Hôtel-Dieu, and the biographical orations threw light on an extraordinary personality. Though his origin was quite humble and his parents were poor, Dupuytren was only 18 years old when he secured the appointment of prosector of anatomy in a Paris school of medicine. This youngster, born in 1777, found himself in a world in which a premium was set on youth, and he was quick to profit by his chance to climb the ladder of fame in short time. Not that his qualifications to do so were flimsy. On the contrary, he made good because of the accurate knowledge of anatomy which he acquired before he was out of his teens. According to Garrison's "History of Medicine," he was the ablest and best trained French surgeon of his time, a shrewd diagnostician, an unrivalled operator, a wonderful clinical teacher, and a good experimental physiologist and pathologist. He was appointed to the staff of the Hôtel-Dieu in 1808, and he became its surgeon-in-chief in 1814. His clinics drew crowds of students from all countries, and his private practice was so great that he saw about 10,000 patients annually outside his hospital. He was the first to excise the lower jaw, to treat aneurysm successfully by compression, and to treat wry-neck by the subcutaneous section of the sternomastoid muscle. He was also a pioneer in the successful ligation of the external iliac and subclavian arteries. His most enduring title to fame is, however, in surgical pathology. His greatest works in this field concern fracture of the lower end of the fibula, congenital dislocation of the hip, and retraction of the fingers due to disease of the palmar aponeurosis, for which he devised an operation. In 1803 he founded the Anatomical Society of Paris, and he generously endowed the well-known Dupuytren Museum. His sexual life, on the other hand, was tragic, and his association with his colleagues a series of spiteful intrigues. Cold, hard, contemptuous, and unscrupulous, he was called by Percy "the first of surgeons and least of men"; he was also known as "the brigand of the Hôtel-Dieu." He died a millionaire and a baron of the Empire, mourned but not loved. But the frankness with which his faults are now discussed is balanced by unstinted tribute to his scientific achievements.

"THE LEGEND OF THE LOW FRENCH BIRTH-RATE"

Vehement protests have greeted Dr. Roubakine's comments on French vital statistics (see THE LANCET, March 9th, p. 571, and March 23rd, p. 702), and within the Academy of Medicine, Charles Richet and E. Rist have replied for a country accused by a Russian guest of being riddled with syphilis and tuberculosis, and saturated with alcohol. Rist was denunciatory rather than documentary, but Charles Richet, though he concluded with a prophetic flight of rhetoric, based it on tables as impressive as Roubakine's. It will be remembered that the critic's main thesis was that it is the French death-rate which is most alarming—not the birth-rate, which is above that of certain other countries, including Germany. To this Richet replies that between 1921 and 1931, some 1,300,000 immigrants, mostly young adults, have streamed into France from neighbouring countries and, by virtue of their youth, have contributed much more to keeping up the French birth-rate than have the native Frenchmen. In other words, the population of France at the present time is being kept up by the second as well as by the first generation of immigrants. As for Roubakine's argument that legislative and economic measures are impotent in relation to the birth-rate, Richet reminds him that in Germany Hitler's provision of grants awarded to large families is reflected in the fact that there were 80,000 more births in the first half of 1934 than in the first half of 1933. Richet believes that if France does not reform her *mores*, her system of taxation and her laws, her coffins will outnumber her cradles.

THE CAMPAIGN AGAINST PROSTITUTION

The vested interests in prostitution are not quite as gilt-edged in their security as they used to be. This is so because the example of Grenoble, whose municipal authorities have declared war on organised prostitution, has recently been followed by several other communities. One of the latest adherents to this movement is the town of Fontainebleau, whose mayor, Dr. Marty, has given orders for the suppression of brothels *et hoc genus omne* as from Jan. 1st, 1935. Women under eighteen are no longer to be allowed to work in cabarets, bars, and the like, and those over this age-limit must be able to produce a certificate of good conduct of recent date. Dr. Marty's measures have also included a reform of the police service concerned with the morals of the town, and he has organised a social hygiene dispensary for the discovery and ambulatory treatment of cases of venereal disease. Another community which has turned on the brothel proprietor is that of Saint-Brieuc, whose mayor has given them notice that failure to close their establishments will spell prosecutions in due course.

The gynæcologist, Dr. Siredey, president of the French Academy of Medicine, has lately expressed his firm conviction that the immediate suppression of brothels would mark an important advance. But such a measure would be effective only, he

thinks, if it were accompanied by proper supervision in the streets and suspect quarters to which prostitutes would shift when expelled from the public brothel. It would also be necessary to conduct a carefully organised campaign in favour of better morals.

SCOTLAND

(FROM OUR OWN CORRESPONDENT)

TOBACCO AMBLYOPIA

AT last week's meeting of the Edinburgh Medico-Chirurgical Society Dr. H. M. Traquair read a paper based on his long experience of tobacco amblyopia. He pointed out that the ganglion cells of the retina or their fibres are extremely susceptible to the action of toxic substances. Some of these affect the peripheral cells, but the majority affect the central cells or fibres, and thus interfere with central vision. Most of the toxins which cause central visual defects also cause peripheral neuritis; but tobacco is an exception. Only the visual elements distal to the chiasma are susceptible, and it is probably the ganglion cells alone that are concerned in all types of toxic amblyopia.

Tobacco belongs to the group of poisons which affect the central nerve elements of the retina. The poison may be absorbed by smoking, chewing, snuffing, or eating tobacco, so that the toxic substance is not necessarily a distillation product. The smoking of a large number of cigarettes usually brings on gastric or cardiac symptoms before amblyopia develops; but if a pipe is smoked, or if the patient chews tobacco, amblyopia may be pronounced while other symptoms of tobacco poisoning are slight. An average of 84 cases of tobacco amblyopia are seen every year at Edinburgh Royal Infirmary, and these constitute 1 per cent. of all eye cases attending the out-patient department. In the past twenty-two years, 1856 cases have been seen in the Infirmary, of which all but 8 were in males. Most of the patients have been between 45 and 65 years of age, and the amount of tobacco consumed has varied from ½ oz. to 9 oz. a week, the average being just over 3 oz. The smallest quantity of cigarettes producing amblyopia was 70 a week.

The clinical diagnosis, Dr. Traquair said, can be made with certainty if proper methods of examination are used. The patient is usually between 50 and 60 years of age, and complains that he is unable to recognise the faces of his friends in the street, or that there is a mist between him and everything he looks at. He is surrounded by a peculiar heavy odour of stale tobacco which indicates the pipe-smoker. Vision may be depressed to 6/60, but may, to the black-and-white test card, be 6/6 to 6/18. The use of Bjerrum's test card which has grey letters on a grey background demonstrates the visual defect much more easily. Careful examination of the visual fields will always demonstrate a scotoma of a characteristic type, and when the vision of one eye is affected by tobacco amblyopia, Dr. Traquair has never failed to demonstrate a scotoma in the other. In all but the most advanced cases the prognosis is good if the patient stops smoking and leads a healthy life, but the amblyopia may continue to become worse for a few weeks or even months before improvement begins.

MONEY FOR EDINBURGH UNIVERSITY

At the half-yearly meeting of the general council of the University of Edinburgh held last week, it was reported that in recent months bequests and gifts made to the University have amounted to £169,000. Included in this sum are a bequest by Miss Alice Leslie Inglis of not less than £25,000 for the encouragement of research and teaching in the subject of child life and health; a gift of £15,000 by Mrs. Stuart Hall for a lectureship in the pathology of diseases of children; a bequest by Miss Grace Margaret Carmichael of about £9900 for the purpose of founding scholarships for the assistance of students; and a bequest by Prof. R. Ramsay Wright, of the University of Toronto, of £3500 for the establishment of a scholarship for the encouragement of research in zoology.

The Lewis Cameron fund is to be administered as follows: £3000 for the establishment of prizes for the best papers on subjects related to bacteriology or to the diagnosis of diseases; £15,000 for the endowment of a teaching fellowship in bacteriology; £15,000 to endow one of the existing lectureships of the department of bacteriology; £10,000 to form a fund for the expenses of research work in bacteriology and the diagnosis of diseases; £10,000 for a fund to provide the medical library with books and periodicals relating to bacteriology, and to the diagnosis of diseases. The remainder of the estate will be used to form the nucleus of a medical buildings extension fund.

M.D. EXAMINATION

The clinical examination for the degree of M.D. is still divided into a major and a minor part. It is, however, no longer necessary to profess a special subject, for both these sections can be taken in clinical medicine. The major part of the examination must be taken in clinical medicine unless the special subject professed is anatomy, physiology, pathology, bacteriology, pharmacology, forensic medicine, public health or midwifery, and gynæcology.

UNITED STATES OF AMERICA

(FROM AN OCCASIONAL CORRESPONDENT)

EMERGENCY MEDICAL RELIEF

A SUFFICIENT experience of emergency medical relief under the provisions of Bulletin No. 7 Federal Emergency Relief Administration has now been obtained to justify an estimate of the success of this system of providing medical care for the indigent sick. It is at least obvious that some day a much more comprehensive plan will be needed. Neither relief administrators nor the medical profession are satisfied with the present provisions. There are two fundamental weaknesses which nobody can dispute: (1) that the distribution of the medical relief is in the hands of laymen; (2) that the funds available are totally inadequate to meet the need. The least unsatisfactory administration has been secured where local medical societies have accepted the budgetary insufficiency as an immutable fact or have taken over the responsibility of providing the administrative machinery. In these cases the doctors do a great deal of work for nothing, but as they are used to working for nothing can at least congratulate themselves on getting some subsidy, however small.

The inadequacy of funds leads to strange rulings. Thus no matter how urgent a person's need, or how completely devoid of resources, he may not be sent to a hospital at F.E.R.A. expense. Most States interpret the ruling to exclude payment of the doctor's fees if he attends a patient in a hospital.

Thus if a doctor wishes to collect a fee for appendectomy he must perform the operation on the kitchen table.

The treatment of syphilis would appear to be allowable on the ground that this disease interferes with earning capacity and also on the ground that it threatens life or health. But on the other hand it is frequently disallowed on the ground that it is a chronic disease. The Colorado relief administration has definitely ruled that "chronic conditions such as diabetes, tuberculosis, cancer, nephritis, venereal disease, epilepsy, &c., are not to be considered our responsibility." This in spite of the fact that Bulletin No. 7 does specifically provide for the treatment of chronic diseases. Furthermore, it appears to be the intention of the Federal administrator and the practice of the State administrators that no one may receive medical aid unless he is already on the list of those receiving material aid. Many a family may be able to buy enough groceries on their regular wage and still have nothing to spare when sickness visits them. These families it seems are not eligible for medical relief, even though the sickness be acute and dangerous. Your correspondent is advised that such probably would be the ruling though he has been unable to obtain any definite ruling from the Federal Emergency Relief Administration.

MEDICINE AND THE LAW

Refreshing the Memory

A LEGAL contemporary has recorded that in Smith *v.* Lowry (the claim against an osteopath summarised in this column on April 6th) a medical witness was allowed to refresh his memory as to the condition of a patient by referring to notes made by one of his pupils. Counsel on the other side objected. As it appeared that the witness had instructed the pupil to make the notes and had read the notes at the time, Mr. Justice Talbot overruled the objection.

A witness is ordinarily prevented from proving any fact by evidence of some previous statement made by himself outside the court. If, however, the statement is a written one, he can refresh his memory of facts formerly within his knowledge by looking at the document. The written statement need not have been made at the very moment of the transaction to which it relates; it is merely necessary that the note should have been made at a time when the witness's recollection of the facts was still clear and distinct. Witnesses have been allowed to refresh their memory by inspecting a note made within a week of the transaction, but not where the note was made six months afterwards. And, as in Smith *v.* Lowry, the note need not have been made in the witness's own handwriting, provided that it was made under his personal observation or was recognised by him as a correct record at a time when the facts were fresh in his mind. So the master of a ship, giving evidence of a voyage, may refresh his memory by reference to entries in the log-book made by the mate, or a tradesman may look at account-books kept by a clerk.

Expert witnesses are allowed to refresh their memory by referring to treatises which they habitually consult. This step does not make the treatise evidence in itself; the witness is obliged to give the result in his own words and on his own responsibility. In cross-examination, of course, an expert witness is often invited to refer to text-books in the hope that he will admit that he is wrong.

THE SERVICES

ROYAL NAVAL MEDICAL SERVICE

Surg. Comdrs. A. de B. Joyce, H. H. Babington, and G. H. Hayes to *President* for Medical Dept., Admiralty.

Surg. Lt.-Comdrs. E. B. Pollard to *Galatea* and to *Pembroke* for R.M. Infirmary, Deal; J. J. Keevil to *Victory* for R.N.B., Portsmouth; D. C. Drake to *Drake* for R.N. Hospital, Plymouth; and J. L. Malone to *Arethusa*.

Surg. Lts. E. James to *Milford* on recommg., and W. J. M. Sadler to *President* for course.

ROYAL NAVAL VOLUNTEER RESERVE

Surg. Lt.-Comdr. R. R. B. Roberts to *Victory*.

Surg. Lts. G. F. S. Parker to *Iron Duke*; R. D. Jenkins to *Victory*; and W. T. R. Chapman to *Durban*.

A. I. L. Maitland entered as Proby. Surg. Lt. and attached to List 1 of the Clyde Division (headquarters).

Proby. Surg. Sub-Lt. K. E. O. Ringdahl to *Renown*.

ARMY MEDICAL SERVICES

Col. H. H. J. Fawcett, D.S.O., h.p., late R.A.M.C., retires on ret. pay.

ROYAL ARMY MEDICAL CORPS

Short Service Commissions.—Lts. (on prob.) R. S. Vine, J. E. Jameson, R. H. Wheeler, and J. J. C. Rainsbury, are confirmed in their rank.

The undermentioned Capts. to be Majs. (Jan. 29th, 1935): J. N. Atkinson and J. D. Corner. (Substituted for notification in the *Gazette* of Feb. 8th, *vide* THE LANCET, Feb. 16th, 1935, p. 398.)

TERRITORIAL ARMY

Capt. F. R. Curtis resigns his commn.

Lt. W. R. Nash to be Capt.

R. W. D. Turner (late Cadet Serjt., Epsom Coll. Contgt., Jun. Div., O.T.C.) to be Lt.

H. W. E. Jones to be Lt.

B. L. McQuillan (late Offr. Cadet, Queen's Univ. Contgt., Belfast, Sen. Div., O.T.C.) to be Lt.

The Efficiency Decoration has been conferred upon Col. A. H. Gosse, Hon. Col. F. Marsh (R.A.M.C. units, 48th (S. Midland) Div.) (Bt. Col. ret. T.F.), and Lt.-Col. and Bt. Col. H. L. Garson.

TERRITORIAL ARMY RESERVE OF OFFICERS

Capt. G. McLoughlin, from Active List, to be Capt.

ROYAL AIR FORCE

Flight Lts. R. E. Alderson to Central Medical Establishment, London., and R. E. W. Fisher, to Aircraft Depôt, Karachi, India.

INDIAN MEDICAL SERVICE

To be Capt. (on prob.): E. C. Hicks.

To be Lts. (on prob.): I. J. Franklen-Evans, J. Duffy, A. W. Sampey, J. Reidy, G. C. Welply, C. L. Greening, C. B. Jones, K. Cunningham, G. F. Adye-Curran (secd.), and J. F. A. Forster (secd.).

DEATHS IN THE SERVICES

Squadron Leader ROBERT BOOG WATSON, who died after a short illness at the West London Hospital on May 2nd, was born in Edinburgh on Christmas Day, 1893, the younger son of Charles V. Boog Watson, an engineer. He was educated at Merchiston School and in France and Germany, but owing to an accident in which he lost a foot he was unable to serve during the late war. He graduated M.B., Ch.B. Edin. in 1919, was house physician to Sir Robert Philip, and then house surgeon at the Royal Infirmary. He joined the medical branch of the Royal Air Force in June, 1920, took the D.P.H. in 1921, and was promoted squadron leader in June, 1930. He served twice in Iraq, and at the time of his death was assistant director (hygiene) at the Air Ministry. His early death is much to be regretted; he was a loyal and zealous officer of a type which can ill be spared. He leaves a widow and one daughter, with whom much sympathy is felt.

PUBLIC HEALTH

RESERVOIRS OF BOVINE TUBERCLE BACILLI: THEIR RELATION TO A SAFE MILK-SUPPLY

By R. H. Parry, M.D., M.R.C.P.

MEDICAL OFFICER OF HEALTH FOR THE CITY OF BRISTOL; PROFESSOR OF PREVENTIVE MEDICINE IN THE UNIVERSITY; AND

I. Walker Hall, M.D.

DIRECTOR OF PREVENTIVE MEDICINE LABORATORIES AND EMERITUS PROFESSOR IN THE UNIVERSITY OF BRISTOL

Although the attainment of tubercle-free herds may appear to some to be a visionary hope, it must be admitted that there is cause for immediate dissatisfaction that the animal returns of laboratories do not point to a falling curve similar to that of human tuberculosis. The administration of the milk and dairies order and the tuberculosis sub-order by local authorities have not resulted in any tangible reduction in the output of tuberculous milk. The problem was, perhaps, too great to be tackled by local authorities on such lines. It is not surprising, therefore, that health authorities are turning to pasteurisation as a means of protecting the public from all the associated risks. Nevertheless, we should not thereby be diverted from the aim to free our herds from tubercle, or at all events, to make greater strides to that end.

While it is customary to express the milk tubercle problem in terms of varying numbers of infected cows or in percentages of tuberculous milks, there is another angle from which the question may be considered, namely, the numbers of infected farms that act as reservoirs for the dissemination of bovine strains.

For instance, during 1934 we found that 5·1 per cent. of 485 samples of milk from one area contained virulent tubercle bacilli. This conjured up the vision of some 23 cows with tuberculous udders. But when the sources of the milk were more closely scrutinised, it was evident that these animals were limited to 14 farms and that the milk therefrom was intermittently tuberculous over several months. Hence it was incumbent to envisage these sources as continuous, or recurrent foci, for the spread of tubercle bacilli via milk, utensils, workers, calves, and other animals in the same farm. In some definite instances it was possible to trace the infection by transfer of the cows to adjacent farms and markets. The potentialities for infection from each of the 14 centres assumed greater proportions than could be dealt with except by measures more systematic than those that to-day are considered to be satisfactory.

DELAY INVOLVED IN PRESENT PROCEDURE

What, in fact, are the actual procedures that at present may follow a report from a consuming centre that bulk milk from a specified source has been proved to contain virulent tubercle bacilli?

The county officials visit the herds concerned, examine the cows individually, condemn what they can upon inspection, and then probably take a few selected samples of milk for laboratory examination. By this means the infection may be cleared, but it is interesting to note how often clinical examination fails to reveal the source of infection even though there is evidence of the definite existence of such a source. Anyhow, the method as a whole usually takes many weeks for completion and during this time the milk remains infected. A few instances may be cited to demonstrate the existence and persistence of these bacillary reservoirs.

Farm A

Dec. Bulk samples contain tubercle bacilli.
Jan. Clinical examination of 11 cows. All healthy.
Feb. Herd divided into groups. Two groups of 3 and 4 cows yield T.B. milk.
Mar. Two of above 7 had gone dry. Of the other 5, one yielded T.B. milk.

Farm B

June. Bulk milk from 45 cows contained T.B.
July. Vet. selected 7 cows for sampling. One milk yielded T.B.
Aug. Bulk samples yielded T.B. All cows grouped. One group = T.B. milk. Two cows of group found to give T.B. milk.

Farm C

April. Bulk milk = T.B.
May. Vet. took sample from selected cow = negative.
Aug. Bulk milk = T.B.
Sept. Herd sampled in groups. One cow gave T.B. milk.
Oct. Herd sold by auction before definite clearing samples could be taken.

Farm D

April. Bulk milk = T.B. +. Vet. selected 4 samples. All were negative.
July. Bulk milk = T.B. +. Vet. selected 4 samples. All were negative.
Sept. Bulk milk still tuberculous.

Farm E

July. Bulk milk = T.B. +.
Aug. ,, ,, = T.B. +.
Sept. ,, ,, = T.B. not found.
Oct. ,, ,, = T.B. +.
Nov. ,, ,, = T.B. not found.
Dec. ,, ,, = T.B. +.

These results may be summarised thus:

Length of time tuberculous milk was supplied before clearance

Farm A	4 months.	Farm D	6† months.
,, B	3 ,,	,, E	6† ,,
,, C	6* ,,		

* Herd distributed before clearance.
† Still tuberculous.

These records may suffice to support a contention that a more comprehensive and combined attack is necessary for the effective eradication of rural foci of tuberculous material. For many months these herds were excreting tubercle bacilli intermittently, or tuberculous animals were being introduced into the herd at frequent intervals, and the infected milk was being distributed. At once, however, when alterations in procedure are suggested, questions of finance introduce apparent difficulties. These, in this matter, are the children of the myopic economist. It is easy to understand the restricting hand of county and civic authorities, for the problem is essentially national. It is less easy to appreciate the lack of prominence attached to the point that, while the producer suffers a small loss when a tuberculous animal is destroyed, this loss is as nothing to the retention of a tuberculous cow in an otherwise healthy herd. The inevitable spread of tubercle bacilli gradually reduces the value of each of the others, and the frankly tuberculous one soon becomes the price of skin and bone. It is not perhaps within the scope of this article to discuss the part played by compensation in this matter. Can the lot of the dairy farmer be classed among the speculation trades, wherein good margins of profit compensate for heavy risks? If not, compensation on a liberal scale must be considered. Surely we have progressed sufficiently to-day to be convinced that the supply of fresh, clean, safe milk at a reasonable cost is a national need to be met by national provision. At all events, it is clearly evident that the present-day methods are inadequate and uneconomical.

SUGGESTED LINES OF ACTION

Apart from the wastage of hardly won food and the costs of damaged health, the score of economy alone is an urge towards the limitation of a persisting spread of tubercle bacilli from known sources of infection. It is permissible therefore to suggest some lines of action that might lead to more effective protection of the industry and community.

1. That when a milk-supply is proved to be tuberculous, neither removal from nor access of animals to that herd should be allowed without a certificate from the district veterinary official.

2. That at the outset of inspection, the milk from each member of the herd should be sampled. That there should be a close coöperation, consultative and operative, between the veterinary officials and available laboratories, in order to determine what further inspections and samplings are necessary.

3. That until the joint examinations indicate the absence of tuberculosis in the herd all the milk produced should be compulsorily pasteurised.

4. That during this period of probation all calves should be carefully supervised and protected. That efficient cleansing and disinfecting of the premises should be carried out at prescribed intervals and that the manure should be treated so as to destroy pathogenic organisms.

While these suggestions may appear more cumbersome on the one hand, and less radical on the other, than tuberculin testing, yet their application should be less disturbing to economic conditions and so meet an objection that is frequently advanced against routine tuberculin reactions.

We have not attempted here to deal with the problems associated with the tracing of infected milks to their particular source. Bulk sampling is a practical proposition in Bristol. It is not so in large cities where milk has been transported in glass-lined tanks containing as much as 3000 gallons of milk, a procedure that aggravates the situation in regard to the dissemination of disease.

It would have been a passing achievement if we could have pointed to the effective clearance of 14 reservoirs of infection in one area. Such it seems is not a possibility under existing conditions. Perhaps, however, our citation of these records may induce other centres to review their own from a similar standpoint. If their observations confirm our findings, they would constitute a tacit submission for an early reconsideration of existing procedures. At the same time they would bring before all those associated with its production the necessity of convincing the consumer that they are unwearying in their aims to provide a consistently safe and clean milk. The success of "milk campaigns" depends largely on such a satisfaction. But in any case one of the essential features of an extended programme for betterment should be an active coöperation between field and laboratory and the arming of both with sufficiently effective financial and controlling powers.

INFECTIOUS DISEASE

IN ENGLAND AND WALES DURING THE WEEK ENDED APRIL 27TH, 1935

Notifications.—The following cases of infectious disease were notified during the week: Small-pox, 0; scarlet fever, 1994; diphtheria, 996; enteric fever, 16; acute pneumonia (primary or influenzal), 1445; puerperal fever, 47; puerperal pyrexia, 124; cerebro-spinal fever, 23; acute poliomyelitis, 1; encephalitis lethargica, 9; dysentery, 7; ophthalmia neonatorum, 84. No case of cholera, plague, or typhus fever was notified during the week.

The number of cases in the Infectious Hospitals of the London County Council on May 4th was 3459, which included: Scarlet fever, 1035; diphtheria, 1422; measles, 24; whooping-cough, 365; puerperal fever, 20 mothers (plus 5 babies); encephalitis lethargica, 269; poliomyelitis, 3. At St. Margaret's Hospital there were 18 babies (plus 7 mothers) with ophthalmia neonatorum.

Deaths.—In 121 great towns, including London, there was no death from small-pox, 2 (0) from enteric fever, 25 (0) from measles, 5 (0) from scarlet fever, 36 (4) from whooping-cough, 32 (10) from diphtheria, 51 (13) from diarrhœa and enteritis under two years, and 137 (15) from influenza. The figures in parentheses are for London itself.

There is a sharp fall in the number of influenzal deaths which are now chiefly concentrated in the northern area. This week deaths were reported from 52 great towns, Manchester reporting 22, Leeds 16, Middlesbrough 10, Salford 5, no other great town more than 3. Hastings and Plymouth each reported one fatal case of enteric fever. Six deaths from measles occurred at Wigan, 5 at Birmingham. Whooping-cough was credited with 5 deaths at Middlesbrough. In no great town were more than 2 fatal cases of diphtheria reported.

The number of stillbirths notified during the week was 290 (corresponding to a rate of 42 per 1000 total births), including 53 in London.

PANEL AND CONTRACT PRACTICE

Unemployment and Medical Benefit

THE most difficult problem in national health insurance at the present time is the effect of unemployment on the scheme. The reduction of income and the increased expenditure on benefits, whether direct or indirect, form a vicious circle which ever since the first attack of post-war depression which began in 1920 has required palliative treatment in the shape of a series of Prolongation of Insurance Acts. In 1928 an attempt was made to put the matter on a permanent basis, but it was soon apparent that the attempt had not solved the problem, and after further Prolongation Acts in 1930 and 1931, the new Act of 1932 dealt with the situation up to the end of 1935 by prolongation of insurance and partial excusal of arrears. Insurance practitioners, particularly those in the depressed areas, have already appreciated some of the effects of this Act in respect of those unemployed insured persons whose title to medical benefit ceased after Dec. 31st, 1933. But an even more serious situation is due to arise at the end of this year when these people expect to lose their contributory pension rights as well. The health and pensions provisions of our scheme of social insurance are so interlocked that it is not always appreciated that there is an essential difference between them. Broadly speaking, the health provisions may be likened to fire insurance where the risk is a potential day-to-day risk, but pensions are more akin to an endowment assurance where the contributions or premiums are to provide for a future claim at age 65, or in respect of the contributor's widow or orphan.

The National Conference of Friendly Societies have had under consideration a scheme for continuing medical benefit to unemployed persons who have been insured for ten years and have paid not less than 400 contributions, so long as they can prove their availability for, but inability to obtain, insurable employment, and the beneficiaries under the scheme would thereby retain their title to pension rights and to certain health insurance benefits. The proposal is that the charge in respect of medical benefit against insurance funds should be a collective responsibility of the National Health Insurance

Fund as a whole and that, in allocating this cost against the approved societies, no regard should be had to the financial positions of the various societies. The foregoing scheme has, however, been adversely criticised, as it is thought not to go to the root of the matter. Various groups of approved societies have given intensive consideration to the question, and it would appear that there is now a certain degree of agreement that arrears might be disposed of by a charge on each society's contribution income, each society in its turn to receive back out of the fund thus created its own measure of relief calculated upon the extent of unemployment amongst its members. This plan would make the unemployment risk a common charge on all types of societies which would vary as the unemployment figures varied. It has been stated that the charge at the present time would represent substantially less than one penny per contribution actually received by societies.

But the scheme, statesmanlike though it is, may have an adverse effect upon additional benefits, dental, ophthalmic, and the like, and so it is not surprising that some voices are already asking as to the possibility of securing a Government grant. This is, however, a matter of politics on which the medical profession as such has no voice, although they may observe with gratification that attempts are being made to preserve not only medical benefit but the other benefits of health and pensions insurance for those who have fallen on hard times owing to continued unemployment. Two groups of societies have recently expressed their readiness to join in providing substantial financial assistance to the 5,000,000 insured persons who are in arrear, due to unemployment, in order that their right to statutory benefits, medical and other, may not be jeopardised.

Supply of Anti-diphtheria Remedies

Some months ago a medical service subcommittee dealt with a case in which an insurance practitioner treated a young dressmaker as a private patient and rendered an account for £6 7*s.* 6*d.* for the period Oct. 30th to Nov. 2nd, but of this amount £4 19*s.* 6*d.* represented his charge for diphtheria antitoxin. There was a conflict of testimony as to when the practitioner was first asked to treat the girl as an insured person. At the hearing the practitioner, who was under the impression that his secretary had paid the local authority for the antitoxin, expressed his willingness to withdraw the account. It was it seems the practice of the local authority in question to supply the antitoxin gratuitously for use in necessitous cases. Under Clause 9 (8) of the Terms of Service a practitioner is required to supply to a patient such drugs and appliances as are required for immediate administration or application, and he may supply any other drug which is administered by him in person. But reference to the appendix to the distribution scheme will show that serums can be paid for only when supplied to patients for whom a supply is not made gratuitously available by any public authority. So far as diphtheria antitoxin is concerned the reason for the proviso is that the Diphtheria Antitoxin Order of August 15th, 1910, is not mandatory but discretionary, and it is for the local authority to decide whether a supply of diphtheria antitoxin shall be made gratuitously available, and to interpret the term "poorer inhabitants." Some authorities supply antitoxin gratuitously to all persons requiring it.

An inquiry was recently addressed to the Ministry of Health as to whether diphtheria prophylactic and the material for the Schick test may be regarded as drugs when required in connexion with the immunisation of insured persons. The reply was that while the Minister has no authority to give a ruling—the question can be authoritatively decided only in the manner furnished by the regulations—he is of opinion:—

(*a*) That diphtheria prophylactic is a drug, the cost of which would form a proper charge on the chemists' fund when ordered on the official prescription form in respect of a "prescribing" patient.

(*b*) That preparations which are used for application to the human body for diagnostic purposes must be regarded as properly chargeable to the chemists' fund in the case of "prescribing" patients or the practitioners' drugs account in the case of "dispensing" patients.

An Uncommon Representation

Under Article 44 of the Medical Benefit Regulations the local medical or panel committee have power to consider any complaint made to them by one insurance practitioner against another involving the efficiency of the medical service, and the committee may make representations to the Minister that the continuance on the medical list of the practitioner against whom complaint is made would be prejudicial to the service. The power thus conferred is very seldom exercised to the extent of suggesting the removal of a practitioner's name. Quite recently Dr. A made complaint that an insured person on his list had been transferred to Dr. B's list without the patient's knowledge or consent. The patient's wife was being attended by Dr. B, who on her second visit to him asked her to produce her husband's medical card the next time she called. It seems that he kept the card and told the woman that when she received the card back with a transfer form attached she should take the medical card again to him. According to her own statement the woman followed these instructions and some time afterwards when in hospital her husband came to visit her, bringing with him a new medical card with the name of Dr. B on it. Dr. B admitted that the letter to the insurance committee applying for consent to transfer at the end of the quarter, which purported to be from the insured person, was written and signed by his housekeeper upon his instructions. He had never seen the insured person, but took the action he did at the wish of the patient's wife. The subcommittee were not disposed to accept his assertion that the wife was anxious for the transfer, and passed a resolution expressing their opinion that his continuance on the medical list would be prejudicial to the efficiency of the medical service of insured persons. The Minister will now appoint a day for the holding of an inquiry. Whatever may be the outcome of this particular case, it is evidently most undesirable for a practitioner to act as the agent of an insured person in the matter of applying for consents to transfer. Practitioners accepting transfers should insist that the application on the medical card or on Part A 1 (the red printed slip) should be fully completed and signed by the insured person concerned. It should be added that it is 13 years since such an inquiry was held at the instance of the London panel committee.

BIRKENHEAD GENERAL HOSPITAL.—During the last eight years no beds have been added to this hospital and the wards are crowded. The pressure is greatest in the women's wards, and many patients are waiting for admission. A few rooms are set aside for paying patients, but the demand has grown from 15 in 1926 to 166 last year, and more provision must be made for such cases.

OBITUARY

JAMES PRAIN STURROCK, M.D. Edin.

THE death occurred on April 24th, at Inverness, of Dr. James Prain Sturrock, a commissioner of the General Board of Control of Scotland. Already a graduate in arts at the university of St. Andrews before turning to medicine, he received his medical education in Edinburgh, graduating as M.B., C.M. in 1897. Ten years later he proceeded to the M.D. degree, which he obtained with honours. The whole of his professional life was spent in institutional or official connexion with the treatment of mental disease. First appointed as senior assistant medical officer in the Stirling District Asylum at Larbert, he became assistant medical officer at the Midlothian and Peebles Asylum and later medical officer to the Perth Prison and State Inebriate Reformatory, being also superintendent of the criminal lunatic department. He was appointed a deputy commissioner of the General Board of Scotland in 1914, and became in 1922 full commissioner. His literary output was considerable and useful, dealing with the relations of mentality to crime, with the influence of inebriety upon those relations, and especially the connexion between feeblemindedness and inebriety. He published in the *Journal of Mental Science*, 1910, arising out of his experiences at Perth, a paper on certain insane conditions to be found among the criminal classes. He wrote on the modern aspects of eugenics in the transactions of the Perth Natural Science Society and followed that with an essay on inebriety and feeblemindedness in the *British Journal of Inebriety* for 1912. These essays were characterised by their practical directions, and were founded upon much and close personal observation.

Dr. Sturrock, whose death occurred suddenly from cerebral hæmorrhage, while conducting an official inspection, leaves a wife and daughter.

DR. AXEL REYN

LATE DIRECTOR OF THE FINSEN LIGHT INSTITUTE, COPENHAGEN

Dr. Axel Reyn, who died at the age of 63 on April 22nd, was, through his work in connexion with, and as successor to, the late Prof. Niels Finsen, widely known in the medical world. He became associated with Finsen in 1897 and was later appointed chief of the dermatological department of the Finsen Institute. He made a well-deserved reputation as a dermatologist and will be remembered for his work in actinotherapy in relation to tuberculosis and especially in the local and general treatment of lupus vulgaris. His knowledge of this disease was profound and his skill in its treatment was widely recognised. Sufferers from lupus flocked to the Finsen Light Institute from all parts of the world, and many will ever have reason to recall with gratitude the success with which they were treated. He devised the Finsen-Reyn lamp, a modification of the original Finsen lamp, which is especially useful for the treatment of individual cases, and has been introduced into hospitals and clinics the world over, where it is still successfully employed. He introduced carbon arc baths for the general light treatment of surgical tuberculosis, and with N. P. Ernst published his method in 1914. In 1913 he published "Die Finsenbehandlung," an important work wherein was collected all existing available knowledge of light therapy, and he wrote numerous valuable papers dealing with lupus vulgaris, and the treatment of X ray burns and ulcers, and of tuberculosis of the glands. Honours came to him plentifully, and he was elected honorary member of many learned societies both in Denmark and abroad. Perhaps the honour he most greatly appreciated was his election as President of the International Light Congress held in Copenhagen in 1932 where glowing and well-merited tributes were paid him by colleagues from many countries, and a special number of *Strahlentherapie* was published in his honour. But already the disease, tuberculosis, which eventually killed him, had attacked him severely, and he resigned the directorship of the Finsen Institute in 1933, being elected president of the board. His successor at the Institute is Dr. Sven Lomholt.

Sir Henry Gauvain, to whom and to Dr. A. E. Kissmeyer, Reyn's friend and colleague, we are indebted for much of this information, writes: "For those who were privileged to know him the death of Axel Reyn creates a great sense of personal loss. His was a modest, lovable personality, generous, always ready to help colleagues, and devoted to the interests of his patients. He was a man of deep culture and wide interests, fond of travelling and particularly of the Mediterranean coast. Of recent years he was in the habit of spending the spring on the Riviera and this year had only returned to Copenhagen three weeks before his death. He married in 1893 Elizabeth Finsen, sister of Niels Finsen; she survives him, but they had no children. Reyn was particularly interested in the promotion of preventive measures against tuberculosis and debilitating diseases in children, and the success which attended his efforts in these directions proves the necessity of their application."

THE LATE GORDON ERNEST ODDIN-TAYLOR, M.R.C.S. Eng.—A South African correspondent sends the following notes upon the career of Dr. Oddin-Taylor, who died recently in Pietermaritzburg, where he was senior surgeon to Grey's Hospital at the time of his death, which followed a serious operation. "Dr. Oddin-Taylor was a member of a well-known Norfolk family and received his medical education at St. Thomas's Hospital, where he qualified with the English double diploma in 1896. He went out to join relatives who were practising in Pietermaritzburg, and for 30 years practised in that town. He was appointed surgeon to Grey's Hospital in 1907, thus serving the institution for the exceptionally long period of 28 years. He had been a member of the old Natal Medical Council and for a long period represented the Natal Inland Branch on the Federal Council. He was held in high esteem by the medical and nursing profession for his skill as a surgeon, and was certainly one of the best known figures in the Natal capital."

MIDDLESEX HOSPITAL.—The Duke of Northumberland has been elected president of this hospital, an office that since the first few years of the hospital's existence has been held by the head of the house of Percy. On the death of the last president the present duke was still a minor, but he has now agreed to continue the tradition of close on 200 years.

HOSPITAL FINANCE AT TAUNTON.—There are now 18,566 contributors to the Taunton and Somerset hospital week's committee scheme, over a thousand more than last year, and the total receipts for the year amount to over £10,000.

CORRESPONDENCE

FLAT-FOOT IN SCHOOL-CHILDREN

To the Editor of THE LANCET

SIR,—I have read with much interest the note on flat-foot in children published in THE LANCET of April 6th (p. 840). I fully agree with Mr. Blundell Bankart that a flat foot is the natural attitude of the foot in relaxation. Indeed, the so-called arch of the foot is its strongest support, but also its largest fault. I also agree with him that the wearing of sandals *might* preserve the natural mobility. But as a result of my investigations I have come to the conclusion that sandals, and especially those with crepe or composition soles, are unsuitable from every point of view. The primary function of a shoe for a growing child is to support the foot, to facilitate walking, and to protect the foot from injury. A sandal is not fitted by its construction to fulfil any of these conditions.

My tests have been carried out with the aid of six children. They showed that the sandals very quickly lost their shape, in some cases within 24 hours. Especially sandals with rubber soles are liable to stretch, the average amount being 5–7 per cent. of the length and 4–5 per cent. of the width. As a result the toe-cap tends to bend upwards and the shoe becomes ill-fitting. It is usual with such footwear for children to wear only thin cotton socks, and in some cases no socks are worn at all. This prevents the shoe from fitting snugly and in my experiments was shown to give rise to inflammation, swelling, chillblains, and abrasions. The investigations carried out by the medical officers in Kent on the relation of heel-less rubber shoes to flat-foot are therefore of great importance. Not only the heel-less shoe, but also the sandal with a slight heel elevation causes within a short time a widening of the foot which accelerates the development of flat-foot.

My impression is the same as Dr. Stableforth's that the proportion of flat-foot in children is much higher in schools where sandals, especially those with rubber soles, are worn than in children who wear leather shoes. In general a pathological condition of the foot is less to be feared in shoes in which the movement of the foot is restricted. Many slight foot complaints develop during adolescence into serious foot complaints. Few children learn the correct way of wearing and standing in sandals, especially those with rubber soles.

I am, Sir, yours faithfully,

Breda, Holland, April 24th. N. C. VAN VONNO.

THE KNEE-JERK IN PNEUMONIA

To the Editor of THE LANCET

SIR,—I feel sure that Dr. Abrahams, having made so many careful observations on this subject, will be interested in Dr. Hughlings Jackson's Neurological Fragments, No. XII, in THE LANCET for 1894, ii, 1472. Dr. Jackson begins his paper—"I have recently found the knee-kerks absent in some cases of croupous pneumonia, absent in three, present in three others. Very likely the absence of these jerks in cases of pneumonia, or in some stages of it, has been noticed before." He then proceeds to give particulars of a case of pneumonia seen with Mr. Wilkin, interesting not only on account of the absence of knee-jerks but also on account of the character of the respirations observed by him. These observations, both of the absence of knee-jerks and of the character of the respirations, were confirmed by Dr. (now Sir Thomas) Barlow, who also saw the patient. In the rest of the "Fragment" Dr. Jackson suggests the spinal cord condition underlying the phenomena which he observed, basing his surmises in what he calls "Gaskell's most important researches."

I am, Sir, yours faithfully,

May 4th. JAMES TAYLOR.

PELLAGRA IN GREAT BRITAIN

To the Editor of THE LANCET

SIR,—In a recent lecture upon nutritional deficiencies reported in THE LANCET last week, Dr. Donald Hunter, under the section Pellagra, makes a statement which I think is calculated to give a wrong impression. He says: "Pellagra is a rare disease in this country. The cases met with are usually secondary to gastro-intestinal disease"—and then goes on to cite Bender, Ellis, and Simpson. The facts are as given in an article upon Pellagra in Great Britain (Quart. Jour. Med., 1934, iii., 10) wherein are summarised all the published cases of pellagra in this country and attention was called to the fact that no case of so-called alcoholic or secondary pellagra had been recorded. Simpson's case, published shortly afterwards, is the only published case of pellagra in this country in which the association of the pellagra syndrome with gross gastro-intestinal lesion has been noted. The cases reported by Bender and by Ellis were American cases. It is not therefore true to say, as Dr. Hunter has suggested, that cases of pellagra in the country are usually secondary to gastro-intestinal disease in the sense in which the statement is used by Bender and other American writers and Simpson.—I am, Sir, yours faithfully,

London, W., May 5th. HUGH S. STANNUS.

PROTEIN SHOCK THERAPY IN TYPHOID

To the Editor of THE LANCET

SIR,—In his letter of Dec. 1st, 1934, Dr. C. E. Price of Toledo (Ohio) mentions my method of treating typhoid fever by protein shock. The shock therapeutics, introduced by Widal in infectious diseases, led in adults in a certain number of cases to an abortive attack with quick recovery. A specific treatment of that kind, viz., the intravenous injection of typhoid vaccine in cases of typhoid, gave in Yoshikawa's hands a rapid recovery after shock symptoms in more than half of the cases after one or two applications. But that treatment, as well as other non-specific cures with intravenous hetero-vaccines and deutero-albumoses, was abandoned after it had happened repeatedly in single cases that the shock was the cause of death. In the course of time it was discovered that not only albumin administered intravenously could prove successful. Such an observation was made by that excellent Viennese clinician, the late Prof. Maximilian Sternberg. In a desperate case of sepsis the 10-fold amount of the usual trypaflavine dose having been given intravenously owing to a miscalculation, a shock of 30 hours' duration was quickly followed by a return to normal temperature and lasting recovery.

These observations led me ten years ago to persevere with the intravenous application of the hypertonic dextrose solutions which I had introduced into therapeutics in 1920 under the name of Osmon (Vienna: Chemosan-Union) and which produce no shock. The sensibilisation usually brought about in

infectious diseases by the bacterial toxins I induced artificially by intramuscular injections of milk (5–10 c.cm.) or of bacterial proteins such as Omnadin or Stormin (Austrian Serum Works). This immunising stimulus, combined with the osmotic stimulus of the dextrose proved sufficient to abort the attack in about 70 per cent. of the cases of lobar pneumonia, typhoid, erysipelas, and Bang's fever. Whenever possible we adminster early in pneumonia and before the fifteenth day in typhoid a dose of albumin intramuscularly, and 20 hours later 20 c.cm. of 50 per cent. dextrose solution with 0·25 mg. strych. nitr. intravenously. In pneumonia fever and pain disappear by the fourth or fifth day after the beginning of this treatment. In typhoid the swelling of the spleen and the abdominal symptoms yield as a rule within four days, the patient becoming afebrile by the sixth day. I have published temperature curves of such cases (Wien. med. Woch., 1931, lxxxi., 254) and Dr. Reinthaller has recently recorded his observations on 160 cases of pneumonia at the St. Pöltner Hospital (Ars Medici, 1934, p. 512). He confirms the quick and sometimes astonishing effect. Pneumonia of the epidemic kind commonly known as influenza (Grippe) reacts less or not at all. Of 90 typhoid cases in my private practice and in hospital I lost only two, one from hyperpyrexia (? after insolation), the other after operation for a wrongly supposed perforation. In the longer cases it was necessary to inject osmon two or three times. Since there is no actual shock this treatment can be carried out at the patient's home if nursing is available.

I am, Sir, yours faithfully,

KARL STEJSKAL.

Spital der Barmherzigen Brüder, Vienna, May 3rd.

NASAL RECONSTRUCTION: THE TUBED PEDICLE FLAP

To the Editor of THE LANCET

SIR,—In reply to Dr. Aymard, I have nothing to add to what you published in the correspondence columns of THE LANCET in August, 1920, in reply to a similar claim by him; *except* to draw his attention to my recent publication re the tubed pedicle in *Surgery, Gynæcology and Obstetrics* in which priority of publication of this flap is given to Filatoff. With regard to the stirrup flap mentioned by Dr. Aymard, I would refer him to Tripier's operation published in the *Revue de Chirurgie*, No. 4, 1890.

I am, Sir, yours faithfully,

Harley-street, W., May 3rd. H. D. GILLIES.

MATERNAL MORTALITY

To the Editor of THE LANCET

SIR,—Mr. Eardley Holland's address to the Royal Sanitary Institute published in your issue of April 27th is most valuable. It is a long time since—in the middle 'seventies—I studied midwifery in Edinburgh under Matthews Duncan who impressed upon us that "festina lente" was to be our guiding motto when attending an expectant mother. For more than 30 years I had a country practice with an average of one confinement a week, 50 miles away from a hospital, and not within easy reach of a medical friend. For some years there were no nurses—only friendly neighbours too eager to be of help, who never learned to understand why I wished my patient not to bear down in the early stage. In tedious cases I was often urged by relatives to use instruments and bring the delivery to an end. This I always resisted, and I gave no chloroform until the second stage was well advanced, stating that if given earlier the pains were weakened and the labour prolonged. There was often great difficulty in making the patient and friends believe this. In using forceps I felt I was acting more safely if my patient was fully conscious, for she would easily show when they hurt her, however gently they were applied. After they were in position she got more chloroform, though in very small amounts. I am therefore in accord with Mr. Eardley Holland on all these points. Nature does the work best, and is much to be preferred to instrumental aid with its risk of injuries to the soft parts. In a busy practice one is often tempted to bring the case to an end, but the question should always be what is best for the patient.

I am, Sir, yours faithfully,

Harrogate, May 6th. JAMES G. MACASKIE.

SUPPLEMENTS TO THE DIET OF CHILDREN

To the Editor of THE LANCET

SIR,—The report recently published by Mr. T. W. Simpson and Mr. Eric C. Wood on the value of supplements to the ordinary mixed diet of children, which is annotated in THE LANCET, May 4th, shows clearly that such mixed diet is deficient at any rate in those factors which make for increased growth. The authors' other conclusions cannot however be accepted without criticism. In the first place, they use as a criterion the weight increase *during* the six weeks during which each supplement is being given. Since growth-factors, whatever their chemical nature, continue to exert their influence for varying periods after they are withdrawn from the diet, it is doubtful if the precaution of giving the different diets in rotation for periods as short as six weeks balances this error. A state of nutrition, as Dr. Magee has recently emphasised, is dynamic, not static, and sufficient time must be allowed for each factor to exert its influence after the effects of the previous one have worn off.

In the second place, the authors conclude that because a "calorie" supplement (vitamin content unstated and unknown) produced better growth than either cod-liver oil or halibut-liver oil and milk, that "balanced calories" are of greater benefit to the child than "vitamins." Since two of the supplements supplied only vitamins A and D, and the third, containing malt, egg, and lemon juice, presumably contained small quantities of the B complex and C in addition, such a sweeping conclusion scarcely seems justified. Vitamins do not fall into a chemical group, and it is as unreasonable to speak of "vitamins" meaning A and D as, for example, of "minerals" meaning only calcium and phosphorus and disregarding iron.

The impression cannot be avoided that different results might have been obtained had the growth factors of the B complex been considered in addition to vitamins A and D.

I am, Sir, yours faithfully,

Wembley Park, Middlesex, May 7th. M. D. WRIGHT.

PUTNEY HOSPITAL.—Princess Arthur of Connaught visited this hospital last week and opened the new nurses' home. Extensions at the hospital have cost £30,000, and there is still a debt of £8000.

OSWESTRY COTTAGE HOSPITAL.—A new cottage hospital is required at Oswestry, and a scheme has been launched for building it at a cost of £20,000. An effort is being made to raise a 10,000 shilling fund.

PARLIAMENTARY INTELLIGENCE

NOTES ON CURRENT TOPICS

Osteopaths Bill: Select Committee's Report

THE meeting of the Select Committee of the House of Lords on the Registration and Regulation of Osteopaths Bill, which had been arranged for Thursday, May 11th, has been postponed sine die on account of the illness of the chairman, Lord AMULREE.

The Committee will meet again at a later date to consider their report.

Ribbon Development

In the House of Lords on Tuesday, May 7th, the Marquess of LONDONDERRY introduced the Restriction on Ribbon Development Bill. The object of the Bill is to provide for the imposition of restrictions upon ribbon development along frontages to roads; to enable highway authorities to acquire land for the construction and improvement of roads; to preserve the amenities or control development in the neighbourhood of roads; to extend the powers of local authorities as to the provision of accommodation for the parking of vehicles and as to the prevention of interference with traffic; and for purposes connected with the matters aforesaid.

The Bill was read a first time.

HOUSE OF COMMONS

WEDNESDAY, MAY 1ST

The New Driving Test

Mr. PARKINSON asked the Minister of Transport the number of persons, male and female, that had been examined for the new driving test; and the number that had failed to satisfy the examiners.—Mr. HORE-BELISHA replied: Up to and including April 27th, 22,539 persons have been examined, of whom 1863 have failed to satisfy the examiners. The periodical returns furnished by the examiners do not distinguish between male and female applicants.

Mr. WEST: Do these figures convince the Minister that there must be an enormous proportion of motorists to-day who are unfit to drive?

Mr. HORE BELISHA: It is the purpose of the test to prevent, at any rate to some degree, bad drivers from getting on to the roads.

Mr. TINKER: Have those who fail another opportunity to undergo a test?

Mr. HORE-BELISHA: Yes, they can certainly submit themselves for a test again after the lapse of the statutory period.

Hospitals and Road Casualties

Mr. LEONARD asked the Minister of Transport the total cost incurred by hospitals in Great Britain in treating road casualties; the amount claimed from his department by these institutions; and the total paid.—Mr. HORE-BELISHA replied: According to a statement in "The Hospitals Year Book, 1935," 25,000 victims of road accidents were treated last year in the voluntary hospitals of Great Britain and Ireland at a cost of £235,000, of which £110,000 was recovered, including £80,000 under the provisions of the Road Traffic Acts and the common law. Payments to hospitals in respect of the cost of such treatment, although they may be made in pursuance of the Road Traffic Act, are not made from funds under my control.

National Health Insurance Funds

Mr. GORDON MACDONALD asked the Minister of Health the total amount of the National Health Insurance funds at Dec. 31st, 1934.—Mr. SHAKESPEARE (Parliamentary Secretary to the Ministry of Health) replied: The amount was approximately £129,500,000.

Mr. MACDONALD: Does the Minister not consider it advisable that some of this amount should be used to safeguard the interests of those who are suffering from the effects of prolonged unemployment?

Mr. SHAKESPEARE: The whole question of unemployment in relation to health insurance is being considered now.

Mr. T. SMITH: Can the Minister say when the promised amending Bill will be introduced?

Mr. SHAKESPEARE: As soon as possible.

Miners' Baths and Welfare Institutes

Mr. LUNN asked the Minister of Labour if a caretaker of a miners' welfare institute or miners' baths was treated as entitled to unemployment insurance benefit in case of unemployment; and whether such cases had been considered by the statutory committee and a recommendation made thereon.—Mr. R. S. HUDSON (Parliamentary Secretary to the Ministry of Labour) replied: Broadly speaking, persons engaged in looking after miners' welfare institutes or miners' baths are regarded, in accordance with judgments given by the High Court, as being employed in domestic service and, therefore, not insurable where they are not employed in a business carried on for the purposes of gain. Both these employments, however, are among those with regard to which inquiries are proceeding with a view to the submission of a draft regulation to the Statutory Committee under Section 2 of last year's Act for the inclusion within the scope of the scheme of certain workers now excepted.

Rural Telephones in Scotland

Sir ARCHIBALD SINCLAIR asked the Postmaster-General in how many cases in the last three years guarantees had been demanded by the Post Office as a condition of extending the telephone in rural districts in Scotland; what was the total amount of such guarantees; in how many cases recourse had been had to the guarantors to make up any deficiency on the cost of the service; and what was the total amount of money paid to the General Post Office in respect of these guarantees.—Sir KINGSLEY WOOD replied: During the past three years guarantees have been required in Scotland in 27 cases, all in connexion with the provision of telephone call offices in rural districts. The total amount guaranteed is £594 10*s.* a year. Nine of the call offices have not yet been in service for a year; but it has been necessary to make demands upon the guarantors in respect of all but one of the remaining 18. These demands number 29 in the period stated; and the total amount paid or awaiting payment is £568 14*s.* 10*d.* As a result of the concession which I announced on April 29th concerning the provision of additional telephone facilities in rural districts, the guarantees in nearly half these cases will be cancelled as from May 1st.

THURSDAY, MAY 2ND

Lifts and Factory Act Control

Mr. RHYS DAVIES asked the Home Secretary if he had considered the question of bringing lifts at residential and office premises under the Factory Acts.—Captain CROOKSHANK (Under-Secretary, Home Office) replied: This suggestion has not been overlooked, but my right hon. friend is not in a position at present to come to any conclusion.

New Water-supply Schemes

Mr. LEVY asked the Minister of Health how much of the Treasury provision for grants in aid of water-supply schemes had been expended; and what was the total expenditure on new water-supply schemes since this provision was made.—Sir HILTON YOUNG replied: The amount of grant provisionally allocated is now £528,000 in respect of schemes of a total capital cost of £3,320,000. It is not possible to state the total expenditure on water-supply schemes since the Act providing the grant was passed in March, 1934, but during this period the loans for such schemes sanctioned by me or by Parliament in local Acts amount to £4,370,000, including £1,400,000 for rural water schemes.

Mr. LEVY: In view of the warning already given by water undertakers, including the Metropolitan Water Board, as to the water shortage this summer, is the right hon. gentleman really satisfied that he is doing all that

can be done to alleviate a water shortage and its consequences ?

Sir HILTON YOUNG : My reply to that question is a suggestion that there is no apprehension of a water shortage this summer.

Expenditure on Social Services

Mr. WEST asked the Chancellor of the Exchequer the total net expenditure in 1934 on social services, excepting sums spent on war pensions.—Mr. CHAMBERLAIN replied : I am afraid that the information asked for is not yet available. As the hon. Member is no doubt aware, full details of expenditure on social services are given in the Return of Public Social Services published each year. The latest issue of the Return (Command Paper 4749 of 1934) contains the figures for 1933, and those for 1934 will be included in the next issue which will be published in the autumn.

Mr. WEST : Is it not a monstrous thing that the figure of £500,000,000, so often quoted in this House, is grossly misleading, and is it not the fact that the increase in social services during the last few years has been largely offset by the increasing taxation borne by the people indirectly ?

Mr. CHAMBERLAIN : I cannot answer that question without notice.

Lieut.-Commander AGNEW : Is it not a fact that we spend each year more than any country in the world on social services and that we get the best results ?

Mr. G. GRIFFITHS : Is it not the fact that there is more stopped out of the wages of the working-class in this country than is the case in any other country ?

No further answers were given.

Hospitals and Milk-supplies

Mr. LEONARD asked the Minister of Agriculture if his attention had been called to the fact that, owing to the regulations of the Milk Marketing Boards, some hospitals had had the price of milk raised against them from 33 per cent. to 63 per cent. ; and to what extent the matter was being considered, so as to assure no limitation of milk consumption in such institutions and no substitution of inferior grades.

Sir JOHN HASLAM asked the Minister of Agriculture what was the reason why hospitals could not purchase the milk they required for their own use at about the same wholesale price as they did before the existence of the Milk Marketing Board.—Mr. ELLIOT replied : As regards the prices payable by hospitals for milk supplied under the Scottish Milk Marketing Scheme, 1933, which were considered by the Committee of Investigation for Scotland, I would refer Mr. Leonard to the reply given on April 8th by the Secretary of State for Scotland. The position in England and Wales is that the Milk Marketing Board have prescribed a form of contract under which hospitals contracting with producers can obtain supplies at the wholesale price with small additional premiums for level deliveries or other special services. Hospitals not contracting with producers may obtain supplies from wholesalers under the resale clauses of the ordinary contract at the wholesale price plus premiums varying from ¼*d.* per gallon for large quantities to 1½*d.* per gallon for small quantities. From particulars furnished by the British Hospitals Association, it appears that as regards approximately two-thirds of the voluntary hospitals in England and Wales the price paid for milk during 1934 was, on the average, about 15 per cent. more than in the year preceding the scheme, but that in individual cases the increase was 33 per cent. and in one instance 63 per cent. I understand that the Association have discussed the matter with the Milk Marketing Board, and that after very careful consideration the Board have not been able to see their way to authorise the sale of milk to hospitals at less than the rates laid down, but they have suggested that if the Association can obtain the concurrence of the Central Milk Distributive Committee (as representing the distributive trade) to the supply at net wholesale prices they will give sympathetic consideration to a variation of the terms of sale accordingly.

Sir JOHN HASLAM asked the Minister of Agriculture, if, in view of the indignation that existed amongst hospital authorities at the high prices they had to pay for their milk-supplies compared with the low prices paid by chocolate and cheese makers, he would take steps to obviate this differentiation.—Mr. ELLIOT replied : My hon. friend will appreciate that the effect of replacing purchases of milk at liquid rates by purchases at the manufacturing prices is to increase the loss already occasioned to milk producers by reason of these prices. I am not quite sure what steps my hon. friend has in mind to meet this difficulty, but I should be glad to consider any proposals he suggests.

Venereal Diseases

Sir ARNOLD WILSON asked the Minister of Health whether his attention had been drawn to the fact that the death-rate from syphilis for 1933 was higher than for 1924, and the total number of reported new cases of venereal disease higher in 1933 than in 1925 or in 1932 ; and whether he would now consider the need for legislation to require compulsory notification and segregation of cases of these infectious and disabling diseases on lines similar to those in force under the Infectious Disease (Notification) Extension Act, 1899.—Sir HILTON YOUNG replied : With regard to the first part of the question, the crude death-rate from syphilis per million persons living was the same in 1933 as in 1924, but the standardised rates show a decline. The numbers of new cases attending the treatment centres provided for venereal diseases show an increase over the years mentioned for all forms of venereal disease, but a decline for syphilis. These figures, however, do not necessarily reflect the actual incidence of the disease. With regard to the second part, I see no reason for disagreeing with the Committee of Inquiry of 1923 which came to the conclusion that compulsory measures on the lines suggested were not desirable in the case of these diseases.

Sir A. WILSON : Is the Minister aware that Great Britain is practically the only large country in Europe where the rates have not shown a very substantial decline ?

Sir FRANCIS FREMANTLE : Does my right hon. friend also realise that Great Britain is the one country where vital statistics are the most real and extensive ?

No further answer was given.

Maternal Mortality, 1934

Mr. GEORGE GRIFFITHS asked the Minister of Health the numbers of deaths from and arising out of childbirth for the year ending Dec. 31st, 1934.—Sir HILTON YOUNG replied : Deaths registered in England and Wales in the calendar year 1934 included 2747 classified to pregnancy and childbearing, and 748 not so classified, but returned as associated with those conditions, amounting in all to 3495. The figures are provisional.

Mr. PIKE : Is my right hon. friend aware that many of these deaths are due to the fact that there is a considerable lack of maternity services throughout the whole of the industrial areas ?

Sir HILTON YOUNG : No, Sir. The suggestion contained in the question is entirely without justification.

Sir FRANCIS FREMANTLE : Has my right hon. friend had his attention drawn to the experiment in Rochdale where as a result of intensive propaganda of existing organisations they were able, in the course of three years, to reduce maternal mortality to about one-third of what it was previously ?

Mr. GRIFFITHS : Is it not a fact that there were 51 more deaths than in the previous year and that the percentage is going up ?

Viscountess ASTOR : Is it not true that people dare not face up to a great many of the causes of maternal mortality, even in the House of Commons, and that until we do face up to some of these causes, such as disease and the lack of birth-control centres, we shall never get down the death-rate ?

Mr. GRIFFITHS : And look after the feeding of the people.

Sir HILTON YOUNG : It has been found to be entirely the case, after investigation, that the causes of maternal mortality are many and varied. It requires most careful investigation into particular cases, and it cannot be ascribed to any single or general cause.

Basement Dwellings in London

Mr. LYONS asked the Minister of Health if any recent investigations had been made into the number and

character of basement dwellings in various parts of London; and the conclusions reached or representations made in the matter.—Sir HILTON YOUNG replied: According to returns obtained by the London County Council last year from the Metropolitan Borough Councils there were in London 20,108 underground rooms habitually used for sleeping purposes which were deemed unfit for human habitation within the meaning of Section 18 of the Housing Act, 1925. As regards the latter part of the question, Clause 71 of the Housing Bill now before this House is designed to extend the powers of the local authorities for dealing with basement dwellings.

TUESDAY, MAY 7TH

Temperature in Hot and Deep Mines

Mr. TINKER asked the Secretary for Mines if he was in a position to make a statement in respect of the temperature in hot and deep mines; and if the Hot and Deep Mines Committee or the Safety in Mines Research Board had come to a decision as to what the maximum temperature should be in mines.—Mr. E. BROWN replied: The matter continues to be the subject of general and practical study by a research committee, and of ameliorative action in particular cases. I have not received any recommendation in favour of fixing a maximum limit of temperature.

MEDICAL NEWS

University of Cambridge

On May 4th the following degrees were conferred:—

M.D.—M. H. Salaman and H. E. Nourse.
M. Chir.—F. W. Holdsworth.
M.B., B.Chir.—A. C. E. Cole, G. E. H. Tisdall, A. T. Blair, H. J. V. Morton, Ashton Miller, G. L. Ward, and L. W. B. Dobbin.
M.B.—E. A. M. Halsted (by proxy), W. H. H. Jebb, H. M. Chappel, P. W. Hutton, J. W. Macmillan, T. M. Bell, W. D. Dick, J. W. Maycock, and A. S. Herington.
B.Chir.—R. J. Buxton.

University of London

On May 28th, 30th, and 31st, at 5.30 P.M., at King's College, Strand, W.C., Dr. Daniel de Lange, director of the Hubrecht Laboratory of the Embryological Institute at Utrecht, will lecture on the head problem in chordates. Prof. J. P. Hill, F.R.S., will take the chair at the first lecture.

Royal College of Physicians of London

Licences to practise (in addition to those given in our issue of May 4th) were conferred by the College upon 84 candidates (78 men and 6 women) who have now completed the final examination of the Conjoint Board and have complied with the College by-laws. The following are the names and medical schools of the successful candidates:—

M. P. Adel, St. Bart.'s; J. K. Adranvala, Bombay and Sheff.; D. G. Allen, Camb. and King's Coll.; Minnie Atkin, King's Coll.; E. B. D. Bangay, St. Bart.'s; A. L. W. Bell, Guy's; M. H. Bob, St. George's; H. V. Brown and J. A. G. Carmichael, Guy's; H. B. C. Carter-Locke, St. Thos.; L. J. Clapham, St. Mary's; J. V. Clark, Guy's; P. E. G. Clements, St. Bart.'s; M. Cohen, King's Coll.; S. Cohen, St. Bart.'s; L. Cooperman, Wits'rand and West Lond.; F. F. Croft, St. Bart.'s; A. P. Dale-Bussell, Guy's; M. C. Damkengrit, Camb. and St. Thos.; Debora David, Royal Free; C. E. M. de Gruchy and G. C. Denny, Guy's; E. P. H. Drake, Camb. and St. Bart.'s; F. P. Ellis, Charing Cross; M. A. Falconer, Otago; J. S. Feynman, Middlesex; J. W. Fisher, Westminster; W. P. Fitch, Guy's; R. J. Force-Jones and L. D. B. Frost, St. Bart.'s; R. T. Gabb, Camb. and St. Bart.'s; J. G. Gladston, St. George's; C. J. Gordon, Camb. and St. Bart.'s; G. B. Grayling, St. George's; K. L. Grogono, London; J. A. G. Hair, Univ. Coll.; J. A. J. Hammond, Guy's; W. F. Harvey, Lond.; T. H. Hills, Guy's; E. D. Hoare, Camb. and St. Mary's; J. J. V. Hopkins and H. M. Hugh, St. Bart.'s; Ruth Hull, King's Coll.; R. F. Jarrett, Camb. and St. George's; J. D. Jenkins, Middlesex; D. V. John, Camb. and Univ. Coll.; I. Klinger, King's Coll.; F. H. Lee, Guy's; D. Levine, Cape and St. Bart.'s; I. W. MacKichan, Camb. and Lond.; P. E. C. Manson-Bahr, Camb. and Lond.; J. H. Mayer, Guy's; M. S. M. Mehta, Bombay and Guy's; H. S. Mellows, Camb. and King's Coll.; W. J. Mitchell and J. F. Morris, Guy's; S. J. Navin, St. Mary's; R. J. Niven, St. Thomas's; W. O. G. Paget, St. Bart.'s; J. H. Patterson, Camb. and St. Bart.'s; S. Phillips, King's Coll.; F. O. Potter, Guy's; A. E. K. Price, Middlesex; G. R. Rawlings, Camb. and St. Thos.; W. M. Rich, King's Coll.; J. S. Richardson, Camb. and St. Thos.; W. B. Ridsdel, Camb. and Lond.; E. P. Rigby, St. Bart.'s; Jean Ross, Univ. Coll.; V. Sankarambal, Madras and Royal Free; J. Schorstein, Vienna and Univ. Coll.; D. S. Scott, Camb. and Lond.; M. J. Shah, Bombay and Lond.; F. A. Simmonds, Camb. and St. Thos.; F. R. Smith, Birm.; J. E. Spalding and D. P. Stevenson, Guy's; K. Tatz, Wits'rand and Guy's; F. Taylor, Guy's; W. Warren, Camb. and St. Bart.'s; C. E. Watson, Camb. and St. Thos.; A. B. Wayte, Guy's; Helen E. Wight, Royal Free; and E. D. H. Williams, Guy's.

National Institute of Industrial Psychology

Under the auspices of this institute three lectures on the temperamental factor in industry are to be given at the London School of Hygiene and Tropical Medicine, Keppel-street, W.C., at 5.30 P.M. on Mondays, May 13th, 20th, and 27th. Prof. Major Greenwood, F.R.S., will deliver the first two, and Miss May Smith, D.Sc., the third. Admission is without ticket.

Jubilee Gifts

Mr. Joseph H. Jacobs has given to St. Bartholomew's Hospital the means to install a new 200 kilovolt X ray therapy apparatus in the radiological department.

Indian Research Fund Association

Dr. Wallace Ruddell Aykroyd has been appointed director of nutritional research under this association.

Ministry of Pensions

Lord Dawson, Sir Farquhar Buzzard, and Sir Lisle Webb have been appointed hon. consulting physicians to the Ministry, and Sir Holburt Waring, Lord Moynihan, and Mr. R. C. Elmslie hon. consulting surgeons.

Glasgow University Club

The London branch of this club will hold a dinner at the Trocadero Restaurant, Piccadilly, W., on Friday, May 31st, at 7.15 for 7.30 P.M., when Lord Macmillan, the president, will be in the chair. The honorary secretaries may be addressed at 62, Harley House, London, N.W.1.

Research Fellowships in Tuberculosis

The Dorothy Temple Cross research fellowships in tuberculosis for 1935–36 will shortly be awarded by the Medical Research Council. The object of these fellowships is to give special opportunities for study and research to workers who intend to devote themselves to the advancement by teaching or research of curative or preventive treatment of tuberculosis. Candidates must be British subjects and must possess suitable medical, veterinary, or scientific qualifications; preference will be given to those who wish to make their studies or inquiries outside Great Britain. The value of the fellowships awarded will not be less than £350 per annum, exclusive of allowances, and they will as a rule be tenable for one year. It may also be possible to award a senior fellowship of considerably greater value to a specially well-qualified candidate who wishes to study some particular problem at a chosen centre in another country. Further particulars and forms of application are obtainable from the secretary of the council, 38, Old Queen-street, Westminster, S.W. 1. Application must be made by June 1st.

Welsh National School of Medicine

Mr. Lambert Rogers, F.R.C.S., reader in surgery at the British Postgraduate Medical School, has been appointed director of the surgical unit of the school and professor of surgery in the University of Wales.

Lambert Charles Rogers qualified M.R.C.S. Eng. in 1920 from the Middlesex Hospital, where he held posts as house surgeon and demonstrator in anatomy. He was then appointed resident surgical officer at the Stockport Infirmary and from there he went to the Welsh National School of Medicine as assistant director of the surgical unit. This post he held until his election last year to the readership in surgery at the British Postgraduate Medical School. Mr. Rogers was the Rogers prize essayist of the University of London in 1921, was proxime accessit for the Jacksonian prize of the Royal College of Surgeons of England in 1931, and was elected a Hunterian professor to the College in 1934 (see THE LANCET, 1935, i., 187). He became M.Sc. Wales and F.A.C.S. in 1928, and F.R.A.C.S. in 1931. His chief contributions to medical literature have been on neuro-surgery and the surgery of the thyroid.

Other appointments made were: Dr. Frank Hawking, assistant lecturer in materia medica and pharmacology; Dr. J. M. L. Burtenshaw, assistant lecturer; Dr. R. W. John, demonstrator in pathology and bacteriology; and Mr. Alan Goode, junior assistant in the surgical unit,

Medical Diary

SOCIETIES

ROYAL SOCIETY OF MEDICINE, 1, Wimpole-street, W.
TUESDAY, May 14th.
Therapeutics and Pharmacology. 5 P.M. (House of the Pharmaceutical Society, Bloomsbury-square, W.C.), Annual General Meeting. Demonstrations: J. Plesch: Tonosciliograph. J. Plesch and E. P. Poulton: Apparatus for Increasing Intrapulmonary Pressure in Treatment of Acute Pulmonary Œdema. M. R. Gurd: Reticulocytes in the Blood of the Pigeon. F. Wokes: Estimation of Thyroid. E. Bülbring and J. H. Burn: Vaso-dilator Fibres in the Sympathetic Supply of the Blood Vessels of the Muscles of the Dog. Communications: K. H. Coward: Effect of Cooking on Amount of Vitamin A present in Vegetables. E. Bülbring and J. H. Burn: Estimation of Œstrone in Oily Solution.
Psychiatry. 8.30 P.M. Annual General Meeting. Dr. C. P. Blacker: The Uses and Limitations of Sterilisation in Social Psychiatry.
THURSDAY.
Dermatology. 5 P.M. (Cases at 4 P.M.) Annual General Meeting. Cases: Dr. Henry MacCormac: 1. Arsenic-resistant Syphilis. Mr. H. Corsi: 2. Case for Diagnosis. ? Lupus Erythematosus. Dr. G. B. Dowling: 3. Sarcoma of the Skin. 4. Morphœa. Other cases will be shown.
Neurology. 7.45 P.M. (National Hospital, Queen-square, W.C.), Annual General Meeting. Cases will be shown.
FRIDAY.
Physical Medicine. 5 P.M. Annual General Meeting.
Radiology. 7 P.M. Annual General Meeting.
Obstetrics and Gynæcology. 8 P.M. Annual General Meeting. Discussion: Diet in Pregnancy. Openers: Dame Louise McIlroy: Diet Requirements in Pregnancy. Dr. G. W. Theobald: The Deficiency Hypothesis of the Toxæmias of Pregnancy. Prof. S. J. Cowell: Calcium Requirement and Calcium Metabolism in Pregnancy.

MEDICAL SOCIETY OF LONDON, 11, Chandos-street, W.
MONDAY, May 13th.—8 P.M., Annual General Meeting. Sir William Wilcox: Toxic Drugs: Their Use and Misuse. (Annual Oration.)

EUGENICS SOCIETY.
TUESDAY, May 14th.—5.15 P.M. (Rooms of the Royal Society, Burlington House, Piccadilly, W.), Prof. R. A. Fisher, F.R.S.: Eugenics, Academic and Practical.

PADDINGTON MEDICAL SOCIETY.
TUESDAY, May 14th.— 9 P.M. (Great Western Royal Hotel, Paddington, W.), Dr. G. P. Crowden and Dr. P. M. T. Kerridge: The Audiometer and Artificial Aids to Hearing.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, 26, Portland-place, W.
THURSDAY, May 16th.—8.15 P.M., Dr. D. H. K. Lee: The Human Organism and Hot Environments.

BRITISH INSTITUTE OF RADIOLOGY, 32, Welbeck-street, W.
THURSDAY, May 16th.—8 P.M., Mr. G. Shearer: The X Ray Microscope. (Presidential Address.)
Medical Section.
FRIDAY, May 17th.—11 A.M., Visit to the X Ray Department of the Middlesex Hospital. 5 P.M., Case Demonstration and Discussion.

ROYAL MEDICO-PSYCHOLOGICAL ASSOCIATION.
THURSDAY, May 16th.—2.30 P.M. (11, Chandos-street, W.), Dr. A. A. W. Petrie: Mental Health Services.

TUBERCULOSIS ASSOCIATION.
FRIDAY, May 17th.—5.15 P.M. (26, Portland-place, W.), Dr. H. P. Nelson and Dr. Peter Edwards: Therapeutic Paralysis of the Diaphragm. 8.15 P.M., Dr. Peter Kerley and Dr. J. V. Sparks: Radiographic Techniques and the Interpretation of Radiographs.

ROYAL MICROSCOPICAL SOCIETY.
WEDNESDAY, May 15th.—5 P.M. (B.M.A. House, Tavistock-square, W.C.), Mr. R. S. Clay and Mr. T. H. Court: The Early Achromatic Objective. Dr. G. M. Findlay: Variation in Viruses.

SOCIETY OF CHEMICAL INDUSTRY.
MONDAY, May 13th.
London Section.—8 P.M. (Chemical Society's Rooms, Burlington House, W.), Prof. F. L. Pyman, F.R.S.: Some Lines of Research in Chemotherapy.

LONDON JEWISH HOSPITAL MEDICAL SOCIETY.
SUNDAY, May 12th.—8.30 P.M. (44, Lancaster-gate, W.), Prof. C. Seligman: Some Aspects of Race Psychology. (Annual Oration.)

LECTURES, ADDRESSES, DEMONSTRATIONS, &c.

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S.W.
TUESDAY, May 14th, and THURSDAY.—5 P.M., Sir Edmund Spriggs: A Clinical Study of Headaches. (Croonian Lectures.)

FELLOWSHIP OF MEDICINE AND POST-GRADUATE MEDICAL ASSOCIATION, 1, Wimpole-street, W.
MONDAY, May 13th, to SATURDAY, May 18th.—BROMPTON HOSPITAL, S.W. All-day course in thoracic surgery.—MAUDSLEY HOSPITAL, Denmark-hill, S.E. Afternoon course in psychological medicine.—ST. JOHN'S HOSPITAL, Leicester-square, W.C. Afternoon course in dermatology. (Open to all.)—Courses arranged by the Fellowship are open only to members and associates.

HOSPITAL FOR SICK CHILDREN, Great Ormond-street, W.C.
THURSDAY, May 16th.—2 P.M., Mr. James Crooks: Infection of the Ear and Sinuses. 3 P.M., Dr. W. W. Payne: Carbohydrate Metabolism.
Out-patient clinics daily at 10 A.M. and ward visits (except on Wednesday) at 2 P.M.

WEST LONDON HOSPITAL POST-GRADUATE COLLEGE, Hammersmith, W.
MONDAY, May 13th.—10 A.M., Medical and Surgical Wards, Genito-urinary Operations, Skin Clinic. 2 P.M., Gynæcological and Surgical Wards, Eye and Gynæcological Clinics.
TUESDAY.—10 A.M., Medical Wards. 11 A.M., Surgical Wards. 2 P.M., Nose, Throat, and Ear Clinic.
WEDNESDAY.—10 A.M., Medical Wards, Children's Wards and Clinic. 2 P.M., Gynæcological Operations and Eye Clinic.
THURSDAY.—10 A.M., Neurological and Gynæcological Clinics. 12 noon, Fracture Demonstration. 2 P.M., Genito-urinary and Eye Clinics. 3.45 P.M., Venereal Diseases Clinic.
FRIDAY.—10 A.M., Skin Clinic. Noon, Lecture on Treatment. 2 P.M., Throat, Nose, and Ear Clinic.
SATURDAY.—10 A.M., Medical Wards, Children's and Surgical Clinics.
Operations, Medical and Surgical Clinics daily at 2 P.M.

LONDON SCHOOL OF DERMATOLOGY, 49, Leicester-square, W.C.
MONDAY, May 13th.—5 P.M., Dr. R. T. Brain: Rodent Ulcer.
TUESDAY.—5 P.M., Dr. H. MacCormac: Treatment of Syphilis.
WEDNESDAY.—5 P.M., Dr. I. Muende: Pathological Demonstration.
FRIDAY.—5 P.M., Dr. W. Griffith: Bullous Eruptions.

CENTRAL LONDON THROAT, NOSE, AND EAR HOSPITAL, Gray's Inn-road, W.C.
MONDAY, May 13th, to SATURDAY, May 18th.—Intensive Clinical Course.

ST. MARY'S HOSPITAL, W.
THURSDAY, May 16th.—5 P.M. (Institute of Pathology and Research), Dr. Igor N. Asheshow: Bacteriophage.

INSTITUTE OF MEDICAL PSYCHOLOGY, Malet-place, W.C.
WEDNESDAY, May 15th.—3 P.M., Dr. H. Crichton-Miller: Anxiety. 4.30 P.M., Dr. Cedric Shaw: Hyperthyroidism.

NATIONAL INSTITUTE OF INDUSTRIAL PSYCHOLOGY.
MONDAY, May 13th.—5.30 P.M. (at the London School of Hygiene and Tropical Medicine, Keppel-street, W.C.), Prof. M. Greenwood, F.R.S.: The Modern Importance of the Temperamental Factor and its Ancient History. (Course of three lectures on the Temperamental Factor in Industry.)

UNIVERSITY OF BIRMINGHAM.
TUESDAY, May 14th.—3.30 P.M. (General Hospital), Dr. E. W. Assinder: V.D. Cases of Interest.
WEDNESDAYS.—3.30 P.M. (Anatomy Theatre, The University, Edmund-street), Dr. Howard Collier: Industrial Dermatitis.
FRIDAY.—3.30 P.M. (Children's Hospital), Dr. W. Carey Smallwood: Diagnosis and Treatment of Chronic Bronchitis and Bronchiectasis in Infancy and Childhood.

UNIVERSITY OF LONDON.
MONDAY, May 13th.—5 P.M. (University College), Dr. D. H. K. Lee: Physiological Effects of Tropical Climate. (First of four lectures.)

UNIVERSITY OF DURHAM COLLEGE OF MEDICINE.
SUNDAY, May 12th.—10.30 A.M. (Newcastle General Hospital), Mr. J. Collingwood Stewart: Abdominal Distension and its Significance.

ROYAL INFIRMARY, Manchester.
TUESDAY, May 14th.—4.15 P.M., Dr. William Brockbank: Lung Cancer.
FRIDAY.—4.15 P.M., Mr. J. P. Buckley: Demonstration of Surgical Cases.

GLASGOW POST-GRADUATE MEDICAL ASSOCIATION.
WEDNESDAY, May 15th.—4.15 P.M. (Victoria Infirmary), Dr. W. Herbert Brown: Skin Cases.

ROYAL INFIRMARY, Dundee.
THURSDAY, May 16th.—3.15 P.M., Cinematograph film: The Science and Art of Obstetrics.

Appointments

ELLIS, G. R., M.B. Camb., M.R.C.P. Lond., has been appointed Hon. Assistant Physician to the General Hospital, Birkenhead.
GRAY, W. A., M.B. Edin., F.R.C.S. Eng., Ophthalmic Surgeon to the Corporation of Barking.
KELYNACK, A. V., M.B. Lond., reappointed Senior Resident Medical Officer to the Royal Free Hospital.
MASTERSON, T. L., M.D. St. And., F.R.C.S. Edin., Resident Surgical Officer to the Huddersfield Royal Infirmary.
McFARLAND, B. L., M.D., M.Ch. (Orth.) Liverp., Hon. Orthopædic Surgeon to the Royal Southern Hospital, Liverpool.
RICHMOND, Arthur, M.B. Victoria, D.P.H., Medical Officer of Health to the Berkshire County Council.

SACHS, LEONARD, M.D. Bern., L.M.S.S.A. Lond., Resident Medical Officer to the Royal Bath Hospital, Harrogate.

City of London Hospital for Diseases of the Heart and Lungs.—The following appointments are announced:—
HUDSON, E. H., M.B. Camb., M.R.C.P. Lond., Out-patient Physician;
WOOD, F. G., M.B., D.M.R.E., Radiologist;
RUSBY, N. L., B.M. Oxon., M.R.C.P., Registrar; and
GRANT, C. A., M.R.C.S. Eng., D.M.R.E., Assistant Radiologist.

Royal Borough of Kensington.—The following appointments are announced:
HUNTER, J. W., M.D. Edin., D.P.H., Deputy Medical Officer of Health and Tuberculosis Officer.
BUCK, Helen, M.B. Lond., D.C.O.G., Maternity and Child Welfare Medical Officer.
DAVIS, H. M., M.B. Liverp., D.P.H., Maternity and Child Welfare Medical Officer.

Certifying Surgeons under the Factory and Workshop Acts: Dr. W. M. MARTIN (Peebles, Peebleshire); Dr. A. H. DRIVER (Leominster, Herefordshire); and Dr. A. MENZIES (Youlgreave, Derbyshire).

Vacancies

For further information refer to the advertisement columns

Aberdeen Royal Hospital for Sick Children.—Ophthalmic Surgeon.
***Banbury, Horton General Hospital.*—Res. M.O. At rate of £150.**
Barnsley, Beckett Hospital and Dispensary.—Cas. O. £250.
Bath, Royal United Hospital.—Out-patient and Cas. O. £150.
***Bedford County Hospital.*—First and Second H.S. At rate of £155 and £150 respectively.**
***Belfast, Forster Green Hospital, Fortbreda.*—H.P. At rate of £150.**
Birkenhead, Clatterbridge (County) General Hospital.—Two Asst. Res. M.O.'s. Each at rate of £150.
Birmingham, Camwell Hall Babies' Hospital.—Res. M.O. At rate of £250.
Birmingham City Maternity and Child Welfare Dept.—Temporary M.O.'s. Each £10 per week.
***Bolingbroke Hospital, Wandsworth Common, S.W.*—H.S. At rate of £120. Also Hon. Phys. for Dis. of Children.**
Bolton Royal Infirmary.—Two H.S.'s. Each £125.
***Bradford, Royal Ear and Eye Hospital.*—H.S. £160.**
Brighton, Royal Sussex County Hospital.—Second Hon. Radiologist.
Burton-on-Trent General Infirmary.—Cas. O. and H.P. £150.
Cambridge, Physiology School.—George Henry Lewes Studentship. £250.
***Cancer Hospital, Fulham-road, S.W.*—Asst. Radium Officer. £350.**
Cardiff, King Edward VII Welsh National Memorial Assn.—Asst. Tub. Physician. £500.
***Cardiff, Welsh National School of Medicine.*—Part-time Demonstrator. £50. Also Jun. Asst. in Medical Unit. £250.**
Central London, Throat, Nose, and Ear Hospital, Gray's Inn-road, W.C.—Third Res. H.S. At rate of £75.
***Chester Royal Infirmary.*—H.S. £150.**
City of London Institution, 2a, Bow-road, E.—Asst. M.O. £250.
Coventry, Gulson-road Municipal Hospital.—Second Asst. Res. M.O. £250.
Coventry and Warwickshire Hospital.—H.S. for Aural and Ophth. Depts. At rate of £125.
Derbyshire Royal Infirmary.—Ophth. H.S. and Anæsthetist. £150.
Ealing Borough.—Asst. M.O. £450.
Evelina Hospital for Sick Children, Southwark, S.E.—H.S. At rate of £120.
***Fulham Hospital, St. Dunstan's-road, W.*—Asst. M.O. £350.**
***Greenwich, Dreadnought Hospital.*—Asst. Radiologist. 50 gns.**
Grimsby Corporation Hospital.—Res. M.O. £350.
***Halifax General Hospital.*—Jun. Res. M.O. £250.**
***Hastings, Royal East Sussex Hospital.*—Hon. Phys.**
Herefordshire General Hospital.—H.S. and Cas. O. At rate of £100.
***Hospital for Consumption and Diseases of the Chest, Brompton, S.W.*—Asst. for Dept. of Pathology. £350.**
***Hospital for Sick Children, Great Ormond-street, W.C.*—H.P. and H.S. Each at rate of £100.**
Hull Royal Infirmary.—Cas. O. At rate of £150.
***Huntingdon Administrative County.*—Asst. County M.O. and Asst. School M.O. £50 a month.**
Indian Medical Service.—Commissions.
Iraq Government.—Appointments. Each £100–£120 per mensem.
***King George Hospital, Ilford.*—Res. Surg. O. and Res. Asst. Surg. O. £300 and £250 respectively. Also Two H.P.'s and Three H.S.'s. Each at rate of £100.**
King's College Hospital, S.E.—Registrar to Ear, Nose, and Throat Dept.
Lincoln County Hospital.—Jun. H.S. At rate of £150.
Liverpool, Cleaver Sanatorium for Children, Heswale.—Res. Asst. M.O. £300.
***Liverpool Sanatorium, Delamere Forest, Frodsham.*—Second Asst. to Med. Supt. £200.**
L.C.C. Cumberlow Lodge School, South Norwood, S.E.—Part-time M.O. £40.
***London Hospital, E.*—1st Asst. to Gyn. and Obstet. Dept.**
Macclesfield General Infirmary.—Second H.S. At rate of £150.
Maidstone, Kent County Ophthalmic and Aural Hospital.—H.S. to Ear, Nose, and Throat Dept. At rate of £200.
***Manchester, Ancoats Hospital.*—Cas. O. At rate of £250. Med. Reg. £50. Also H.S. At rate of £100.**
***Manchester, Monsall Hospital for Infectious Diseases.*—Asst. M.O. £350.**
***Manchester, Park Hospital, Davyhulme,*—Res. Surg. O. £500.**
***Manchester Royal Infirmary.*—Jun. Asst. M.O. in Radiological Dept. £350. Also M.O. to Out-patients. £35.**
***Manchester, Victoria University.*—Sir Henry Royce Research Fellowship. £500.**
Manchester and Salford Hospital for Skin Diseases, Quay-street.—Two Asst. M.O.'s. Each £100. Also H.S. At rate of £100.
Miller General Hospital, Greenwich-road, S.E.—Out-patient Officer and Two Cas. O.'s. Each at rate of £150. Also H.P. and H.S. Each at rate of £100.
***National Hospital for Diseases of the Nervous System, Queen-square, W.C.*—Registrar. £200.**
Newcastle-upon-Tyne Eye Hospital.—Jun. Res. H.S. £150.
Northampton County Mental Hospital, Berrywood.—Jun. Asst. M.O. £350.
***Oswestry, Robert Jones and Agnes Hunt Orthopædic Hospital.*—H.S. At rate of £200.**
Oxford, Wingfield-Morris Orthopædic Hospital.—H.S. £100.
Plymouth, Prince of Wales's Hospital, Devonport.—H.P. and Cas. O. At rate of £100. Also Res. Surg. and H.S. At rate of £200 and £120 respectively.
***Preston, Sharoe Green Hospital.*—Sen. Asst. Res. M.O. At rate of £150.**
***Queen Charlotte's Maternity Hospital, Marylebone-road, N.W.*—Asst. Res. M.O. At rate of £80.**
***Radium Institute, Riding House-street, W.*—H.S. At rate of £150.**
Reading, Royal Berkshire Hospital.—Cas. O. and H.S. Each £125.
Royal College of Surgeons of England.—Two Examiners in Dental Surgery. Also Court Examiners.
Royal Free Hospital, Gray's Inn-road, W.C.—First Asst. in Children's Dept. At rate of £115.
Royal Northern Hospital, Holloway, N.—Res. M.O. £370. Also H.S. and H.P. Each at rate of £70.
Royal Waterloo Hospital for Children and Women, Waterloo-road, S.E.—Cas. O. £200. Also H.S. At rate of £100.
St. George-in-the-East Hospital, Raine-street, E.—Asst. M.O. £250.
St. Giles' Hospital, Brunswick-square, S.E.—Clin. Asst. At rate of £150.
***St. Helens County Borough.*—Deputy M.O.H. £700.**
St. James' Hospital, Ouseley-road, S.W.—Asst. M.O. £250.
St. Luke's Hospital, Sydney-street, S.W.—Asst. M.O. £350.
***Sheffield Royal Infirmary.*—H.P. At rate of £80. Also Clin. Asst. £300.**
Southampton, Royal South Hants and Southampton Hospital.—Cas. O., Res. Anæsthetist, and H.S. Also H.S. Each at rate of £150.
Southend-on-Sea General Hospital.—Med. Reg. £300. Surg. Reg. £250. Also Cas. O. At rate of £100.
Southend-on-Sea, Infectious Diseases.—Asst. M.O. £600.
***South Shields, Ingham Infirmary.*—Sen. and Jun. H.S.'s. £200. and £150 respectively.**
Stoke-on-Trent, Longton Hospital.—H.S. £160.
***Sunderland Royal Infirmary.*—H.P. and H.S. Each £120.**
Talgarth, Breconshire, Mid-Wales Counties Mental Hospital.—Asst. M.O. £350.
Taunton and Somerset Hospital.—H.S. At rate of £100.
Truro, Royal Cornwall Infirmary.—H.S. £170.
***University College Hospital Dental School, University-street, W.C.* Demonstrator in Mechanical Dept. £200.**
Wembley Urban District Council.—Part-time Clinic M.O. £1 11s. 6d. per session.
West End Hospital for Nervous Diseases, Regent's Park.—Hon. Anæsthetist.
West Bromwich and District General Hospital.—H.P. At rate of £200.
Wolverhampton, Royal Hospital.—H.S. At rate of £100.
Wolverhampton and Midland Counties Eye Infirmary.—H.S. £150.
***Woolwich and District War Memorial Hospital, Shooters Hill, S.E.* H.P. and H.S. Each at rate of £100.**
York City.—Sen. Asst. School M.O. Also Asst. School M.O. Each £500. Also Temp. Asst. M.O. £500, and Temp. Res. M.O. £250.

The Chief Inspector of Factories announces a vacant appointment for a Certifying Factory Surgeon at Llanberis, Caernarvonshire.

Births, Marriages, and Deaths

BIRTHS

ATKINS.—On April 29th, at Devonshire-place, W., the wife of Hedley Atkins, F.R.C.S. Eng., of a son.
HODGKINSON.—On May 5th, at Lymington, Hants, the wife of H. Ll. Hodgkinson, M.R.C.S. Eng., of a son.

MARRIAGES

BERRY—INGRAM.—On May 4th, at the Parish Church, Wimbledon, Sir James Berry, F.R.C.S. Eng., of Wendover, to Mabel Marian, daughter of the late T. Lewis Ingram and Mrs. Ingram, of The Priory, Wimbledon Common.
TWEED—HOGGE.—On May 2nd, at St. Matthew's, Ealing, W., James G. Tweed, M.B. Belf., to Betty Josephine Hogge.

DEATHS

BROOKS.—On April 28th, Francis Augustus Brooks, M.D. Brux., M.R.C.S. Eng., of Lonsdale-road, W., in his 73rd year.
FFENNELL.—On May 3rd, at Walton, Clevedon, Edward Barrington Ffennell, M.D. Dub., aged 72 years.
STAMFORD.—On May 4th, suddenly, at Loughborough, Robert Basil Stamford, F.R.C.S. Edin.
WALKER.—On April 30th, Horace Walker, M.R.C.S. Eng., late of Hammersmith.
WHARRY.—On April 27th, at Whitstone Head, Holsworthy, N. Devon, Robert Wharry, M.D. Aberd., in his 82nd year.

N.B.—A fee of 7s. 6d. is charged for the insertion of Notices of Births, Marriages, and Deaths.

NOTES, COMMENTS, AND ABSTRACTS

GUY'S HOSPITAL: PROFITABLE ENTERPRISE

AMONG the statements of account which have recently been presented to the governors of Guy's Hospital on the working of the year 1934, one deals with the cost of feeding the nursing, administrative, and domestic staff of the hospital. It is stated that though the food provided is generous and of good quality, containing a substantial allowance of meat, fish, butter, and plenty of eggs, vegetables, and other foodstuffs, yet the cost to the hospital of feeding its nursing and other staff works out at only 6*s*. 6*d*. a week per head. It is clear that, even when the reduction in price of food bought in large quantities is taken into consideration, good and sufficient food cannot be provided at such a low cost without very wise buying and expert handling of materials. Another statement shows that the whole cost of housing the nurses, including repairs and maintenance of the nurses' homes, insurance and rates on them, wages of maids, renewals of furniture, bedding, hardware and crockery, cleaning materials, staff uniforms, and laundry, works out at a fraction less than 10*s*. a week per head. At this hospital, at any rate, the emoluments of the probationers and nurses amount to less than the rate of £50 a year at which they are assessed in the Federated Superannuation Scheme for Nurses and Hospital Officers.

A statement is also made on the year's working of Guy's Hospital shop. This was started a few years ago in a kind of large kiosk in the hospital grounds for the benefit of patients and nurses, and is now quite a flourishing little business, making a profit for the hospital funds. The shop sells all manner of goods likely to be needed by patients, who send their orders from the wards by their visiting relations, or by voluntary helpers who take trays of things like sweets and tobacco, and lists of other items stocked by the shop, round the wards from time to time. The stock includes biscuits, cakes, and light foodstuffs, including ice-cream, all kinds of haberdashery, and articles of clothing such as night-wear, bed-jackets, or such garments as patients brought into the hospital unprepared, or staying longer than they had anticipated, might need. The account for the year 1934 shows that the shop, after paying all expenses—salaries, repairs, electricity, gas and water, cleaning, rent, and rates—made a profit on trading of 19·5 per cent., which represents £462 19*s*. 1*d*. in cash.

Another profit-making section of the hospital is its paying patients' ward, a pioneer institution of its kind, having been first started over 30 years ago. From a financial point of view the ward is run as a separate unit, and when all expenses, including rent, rates, and taxes, and proportion of administration, have been deducted from income, the profit for the year 1934 is shown as over £3000.

Still another successful enterprise of Guy's is its electricity generating station, which supplies all current required for the manifold demands of this great hospital at a cost which works out at approximately 0·7*d*. a unit.

THE LEVEL OF AMPUTATION

WE have already summarised some of Prof. René Leriche's invective against rapid amputations slavishly reproducing those of the operative surgery class (Jan. 5th, p. 38). In the same paper he pointed out that amputation in the presence of local circulatory failure has problems of its own, and unless there is moist gangrene and spreading septic infection it rarely need be looked on as an emergency operation. There is time, he said, to consider in detail the indications for amputation at a particular level; and sometimes it is profitable to try to increase the efficiency of the circulation and thus the chances of successful healing at a lower level.

Writing on the same subject last year, R. W. McNealy and Philip F. Shapiro (Surg., Gyn., and Obst., 1934, lix., 650) suggested that safety is too often sought by amputating above the knee, where a careful investigation would have saved the patient from a needlessly mutilating operation. In at least one class of case—commencing gangrene of the toes in thrombo-angiitis obliterans—this consideration is of great importance, for the patients are often young and active. The other two main causes of local vascular failure are arterio-sclerosis and diabetes; and here, of course, general principles of saving life may come before attempts to save six inches or more of a limb which the patient is never likely to put to much use. The type of gangrene in diabetes which is infective in origin is, however, to be distinguished from that due to early arterio-sclerosis, since it does not necessarily require more than a limited amputation.

McNealy and Shapiro gave a detailed account of the tests they use in deciding on the level of amputation. The decision most often lies between amputation of a toe, amputation through the leg 6–9 inches below the knee-joint (which is the best level) or at 4–6 inches (which gives a good enough stump), or amputation through the thigh. They dismiss amputations between these levels as not being very useful in fitting the artificial limb. A good idea of circulatory efficiency can usually, they find, be gained from the history and clinical tests. Amputation below the knee, for example, is likely to be feasible if pulsation is palpable in the popliteal artery, and if the temperature and colour tests are good as far down as the ankle. The colour test is especially important; the limb is raised and the level of the anæmia noted, as also the level of the rubor appearing when the limb is dropped. Two special methods have also proved helpful. An oscillometer is used to decide the level of pulsatile *collateral* supply, as distinct from palpable pulsation in the large vessels; and histamine solution (1 : 1000) is injected intracutaneously because it will produce definite skin changes only in an adequately vascularised zone. These changes are a cyanotic flush, a hyperæmic flare, and finally a weal.

A HANDY EPIDIASCOPE.—The cost of an epidiascope, in many cases the main objection to its installation, has been further reduced by Messrs. Newton and Co., of Wigmore-street, London. The "Wigmore" Epidiascope, a satisfactory instrument for class-room purposes, can be obtained for about £16. Its projection distance may be as great as 14 feet, and a picture as large as 7 feet in diameter can be produced. This will no doubt be a valuable addition to the epidiascopes of British manufacture now available at a reasonable price.

HUTCHINSON'S TECHNICAL AND SCIENTIFIC ENCYCLOPÆDIA, in three volumes of which the first is before us, has been planned to supply the student and the teacher with a description of processes that will enable them to understand how science is applied in industry. The work covers a very wide field, and the articles which vary from a line or two to four or five pages, are from the pens of acknowledged experts. The book is edited by Mr. C. F. Tweney, already well known in the production of similar compilations, and Mr. I. P. Shirshov, A.M.I.E.E., to whom readers who desire a reference to additional sources of information will be grateful for the bibliography promised them at the end of the completed encyclopædia. Medicine is only dealt with incidentally, the article on bacteria, for instance, being concerned with industrial processes rather than disease, but there are short but useful paragraphs under such headings as Adrenalin, Antiseptics, Carotene, Cod-liver Oil, and so forth, and we learn that Annatto is used chiefly for colouring cheese and butter—although it is now illegal in milk. This volume of the Encyclopædia contains 672 pages and costs 28*s*.